

# Probio Mood SAP

Science-based probiotics for mood balance\*

Extensive research regarding gut-brain-axis has revealed a two-way communication between the gut and the brain, facilitated by microbial flora. Gut microbiota has proven to play a significant role in digestive disorders, skin diseases and immune function.\* Recent clinical trials have shown that specific *Lactobacillus* and *Bifidobacterium* strains are capable of regulating mood imbalances, stress, anxiety and depression. The unique combination of *Lactobacillus helveticus* R0052, *Bifidobacterium longum* R0175, and *Lactocaseibacillus rhamnosus* R0011 has been clinically proven to work synergistically to modify microbial flora, and alleviate symptoms associated with stress and can potentially help alleviate anxiety and depression and improve mood balance.\* Specifically, *L. helveticus* R0052 and *B. longum* R0175 have been shown to be able to reduce tryptophan degradation and increase tryptophan synthesis, thereby improving serotonin levels which help alleviate symptoms of depression.\* With the ability to exert hormonal regulation and influence the central nervous system, this unique probiotic strain combination works to improve mental health by fostering a healthy gut-brain relationship.\*

**Probio Mood SAP** can help alleviate anxiety and depression and improve mood balance by positively modulating gut microflora.\*

## SUPPLEMENT FACTS

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
Vitamin C (ascorbic acid)	1.2 mg	1%
Probiotic Blend	300 mg (10 Billion CFU)	**
<i>Lactobacillus helveticus</i> R0052	5 billion CFU	**
<i>Lactocaseibacillus rhamnosus</i> R0011	4.5 billion CFU	**
<i>Bifidobacterium longum</i> R0175	0.5 billion CFU	**

\*\*Daily Value not established

**Other ingredients:** Potato starch, inulin, arabinogalactan, vegetable magnesium stearate, saccharose, maltodextrin, yeast extract (peptone), hypromellose, hypromellose acetate succinate, and purified water.

**This product is non-GMO and vegetarian friendly.**

**Contains no:** Gluten, wheat, eggs, citrus, preservatives, artificial flavor or color.

**ProBio Mood SAP** contains 60 enteric capsules per bottle.

**Keep refrigerated.**

## DIRECTIONS FOR USE

**Adults :** Take 1 capsule daily or as directed by your healthcare practitioner. Take at least 2-3 hours before or after antibiotics.

## INDICATIONS

**Probio Mood SAP** can help:

- Moderate general feelings of anxiety\*
- Promote a healthy mood balance\*
- Reduce stress related gastrointestinal complications like abdominal pain, nausea and vomiting\*

## CAUTIONS & WARNINGS

If you have fever, vomiting, bloody diarrhea or severe abdominal pain, consult a healthcare practitioner prior to use. Stop use and consult a healthcare practitioner if symptoms of digestive upset (e.g. diarrhea) occur, worsen, or persists beyond 3 days.

**This product has come into contact with milk and soy. Do not use this product if you have a milk or soy allergy.**

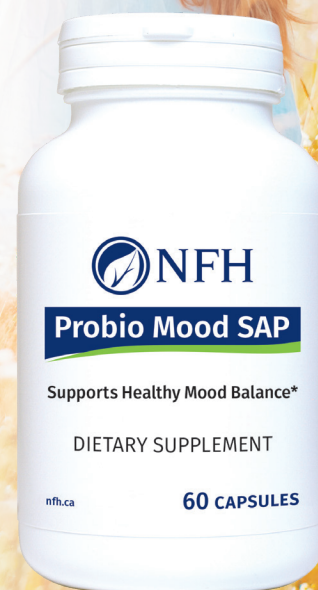
**Contraindications:** Do not use this product if you have an immune-compromised condition (e.g. AIDS, lymphoma, patients undergoing long-term corticosteroid treatment).

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **ProBio Mood SAP** have been tested by an ISO 17025 accredited third-party laboratory for identity, potency and purity.

**\* 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.**

Scientific Advisory Panel (SAP):  
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**GUT BRAIN AXIS**

It has been well established through extensive research that there exists a close relationship between the brain and the gut, modulated by the wide variety of strains of bacteria residing in the gut. Commonly referred to as the brain-gut axis (GBA), this relationship has proven to play a significant role in our health. While research into this area goes back as far as the 1880s, more recent studies point to a two-way communication pathway between the gut and the brain. As Liang et. al. aptly put it, the gut microbiome not only develops in conjunction with the brain, but influences neural pathways and mental perceptions, thereby influencing the pathophysiology of mood and mental disorders. [1]

Microorganisms inhabiting the digestive tract amount to a mass of more than 1kg, that work symbiotically with the brain to regulate pain perception and response, cognitive functions, mood and temperament modulation, and stress management. [1] Studies have found that the microbiota influences the brain by regulating neurogenesis, neurotropic signaling systems and synaptic transmissions, specifically signaling the brain through the vagus nerve. [2] Probiotic bacteria administration can reduce inflammation by altering levels of pro and anti-inflammatory cytokines that directly affect brain function and immune response. Additionally, gut signaling also involves release of peptides that modulate hormone signaling pathways, which help regulate appetite, and production of short chain fatty acids that stimulate the sympathetic nervous system. [3]

**PSYCHOBOTICS: PROBIOTICS AND MOOD DISORDERS**

The most compelling evidence of the use of probiotics as therapeutic agents in the treatment of mental disorders and mood imbalance stems from human clinical trials. In a clinical study conducted with 112 depressed patients compared with 28 normal participants, it was observed that depressed patients had higher levels of immunoglobulins directed against commensal gut bacteria compared with normal patients. Depressed patients showed higher levels of IgA and IgM, with higher levels of IgM in patients suffering from chronic depression. [4]

Liu et. al. conducted a systematic review and meta-analysis of 29 clinical trials administering probiotics and measuring anxiety and depression as the clinical outcome. Administration of *Lactobacilli* alone or in combination with *Bifidobacterium* significantly reduced symptoms of depression in 23 trials with probiotic administration for over a month, accompanied with lower anxiety observed in 22 trials. [5] It is due to these beneficial effects that probiotics have also been termed as 'psychobiotics', since they provide benefits to patients suffering from mood disorders. Several mechanisms of action have been proposed including mediation via the vagus nerve, neuroendocrine systems and regulation of the hypothalamus-pituitary axis. [6]

***Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175**

Clinical studies supplementing with a combination of specific probiotic strains show a synergistic effect on the gut brain axis. A double-blind randomized placebo-controlled study observed the effects of administration of *L. helveticus* R0052 and *B. longum* R0175 on stress related symptoms in 75 participants. Administration of  $3 \times 10^9$  CFU per day for 3 weeks significantly reduced stress-induced abdominal pain, nausea and vomiting. [7]

A stronger and more direct link between these probiotic strains and their amelioration of mental disorders was established by Messaoudi et. al., where administration of *L. helveticus* R0052 and *B. longum* R0175 at a dosage of  $3 \times 10^9$  CFU per day for a month to 66 volunteers showed a reduction in psychological distress, particularly lower anxiety and depression. [8] An open label study conducted with 10 participants over 8 weeks showed remarkable improvements in clinical symptoms of depression, including mood and anhedonia improvement by week 4, and sleep quality improvement by week 8, upon administration of *L. helveticus* R0052 and *B. longum* R0175  $3 \times 10^9$  CFU per day. [9]

It has been hypothesized that one of the mechanisms of action of probiotics consists of influencing tryptophan metabolism by decreasing enzyme activity that contributes to tryptophan degradation in the kynurenine pathway, and synthesizing tryptophan synthase which increases tryptophan production, thereby improving serotonin levels, leading to reduction in depression symptoms. [10, 11] This was demonstrated in a double-blind randomized clinical trial with 81 participants, where a dose of  $\geq 10 \times 10^9$  CFU per day of *L. helveticus* R0052 and *B. longum* R0175 for 2 months showed a significant decrease in depression scores compared with the placebo group, coupled with a decrease in kynurenine/tryptophan ratio. [12]

***Lactobacillus helveticus* R0052 and *Lactocaseibacillus rhamnosus* R0011**

Several studies have looked at the beneficial effects of *L. rhamnosus*, specifically with regards to amelioration of anxiety and depression symptoms. An animal study demonstrated that administration of *L. rhamnosus* in mice regulated emotional behaviour and GABA receptor expression via the vagus nerve. [13] In addition to *L. helveticus* R0052 and *B. longum* R0175, a combination of *L.*

*helveticus* R0052 with *L. rhamnosus* R0011 has shown a synergistic effect in improving the gut microbial environment. A combined dose of *L. helveticus* R0052 and *L. rhamnosus* R0011 ( $2 \times 10^9$  CFU per day) has been shown to maintain better bowel frequency with antibiotic usage, improving symptoms of antibiotic associated diarrhea, in a randomized trial conducted with 172 participants for 14 days. [14] Interestingly, post market research of this combination revealed that these strains protected the gut barrier by adhering to epithelial cells, aiding the expulsion of pathogens and down-regulating inflammatory markers such as IL-1 $\beta$ , IL-8 and TNF- $\alpha$ , thus improving stress management and outcomes. [15]

Clinical studies conducted using this combination indicate an improvement of gastrointestinal diseases triggered by *Helicobacter pylori* and *Clostridium difficile* infections in children, as well as management of atopic dermatitis and vaginal dysbacteriosis. [15] Preclinical studies have helped to establish a more direct link between these probiotic strains and early life stress. Administration of *L. helveticus* R0052 and *L. rhamnosus* R0011 improved emotional learning in infant rats exposed to early life stress [16]. Supplementation with this same combination improved and even reversed generational effects of stress induced by emotions such as fear in animal models. [17] These effects have been observed not only in early infancy, but also in puberty onset and development, where stress induced puberty onset is earlier in females and later in males compared to their counterparts not exposed to the same stress. Administration of these probiotic strains helped in restoring normal onset of puberty in animal models. [18]

**A SYNERGISTIC APPROACH**

Based on the aforementioned clinical evidence, a synergistic combination of the three strains *L. helveticus* R0052, *B. longum* R0175 and *L. rhamnosus* R0011 could be used as an efficacious and safe therapeutic option to improve mood balance and help alleviate stress and anxiety and address related gastrointestinal disorders.

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