



White Paper

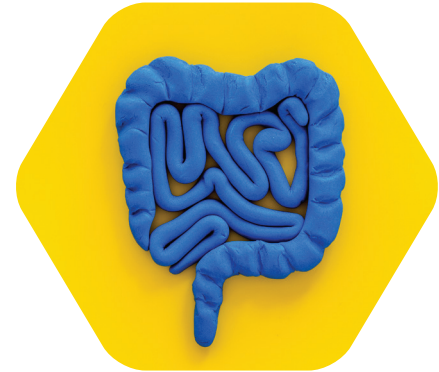
Lactobacillus plantarum

DR7

Next Generation Probiotic for Enhanced Gut and Brain Health

* 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.

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The Importance of Choosing Well When it Comes to Gut

The Gut is the Gateway for our Overall Well Being

The core of overall well-being is maintaining good emotional and physical health, which often comes down to enhancing our digestive and immune health.

In recent years, links between digestive health, brain health, the immune system, mood and mental health has been demonstrated by an expanding body of research revealing the role of the microbiome in supporting the evidence of this unique connection.

Our "gut brain" influences both digestive and immune health and certain probiotic strains may have a positive effect on both healthy digestive and immune function, helping to support overall wellness.

The present white paper explains how stress and anxiety can contribute to gastrointestinal disturbance, and also how gut microbiota can impact our mental health. It summarizes the outcome of *Lactobacillus plantarum* DR7 probiotic for the improvement of stress and anxiety with respect to microbiome change, inflammation, and stress pathway.

Understanding the Gut-Brain Axis

The Brain-Gut Connection: How the Gut and Brain Work Together?

There is a real connection between gut and mind. The gut-brain axis is the two-way communication system between the brain and belly. This axis maintains the body's state of steady functioning known as homeostasis.

The underlying mechanism of probiotic-mediated improvement of mental health is not fully illustrated, even though some studies explained that the microbiota-gut-brain axis signaling can occur via several pathways, including via the immune system, recruitment of host neurochemical signaling, direct enteric nervous system routes and the vagus nerve, and the production of bacterial metabolites.

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Influence of Probiotics on Cognitive Function & Wellness

Microbiota-Gut-Brain Axis: New Therapeutic Opportunities

Targeting the gut microbiome, by the use of probiotics, could restore the gut barrier function, reduce systemic inflammation and could have a beneficial effect in reducing stress and anxiety.

Major recent breakthroughs in science confirmed the important role of gut-brain in physical and mental health. It indicates that the gut microbiota influences the brain development and the behaviours of the host through the gut-brain axis.

The gut-brain axis describes the connection between the brain and the gut. It is a bidirectional communication system that integrates neural, hormonal and immunological signalling between the gut and the brain. Actually, the gut counts millions and millions of neurons that connect with the brain. The gut also hosts an important part of our immune system. This immune system communicates with the whole body, including the brain, through different molecules.

Direct targeting of the gut microbiome with probiotics is a great opportunity toward a new generation of therapeutic options with superior safety profiles for nervous system disorders through maintaining a healthy digestive system.

However, it is also becoming more apparent that targeted alterations in microbiota-gut-brain axis signaling represent a real therapeutic opportunity for adjunctive probiotic supplementation for a number of cognitive applications, particularly in instances of stress, anxiety, and memory support.

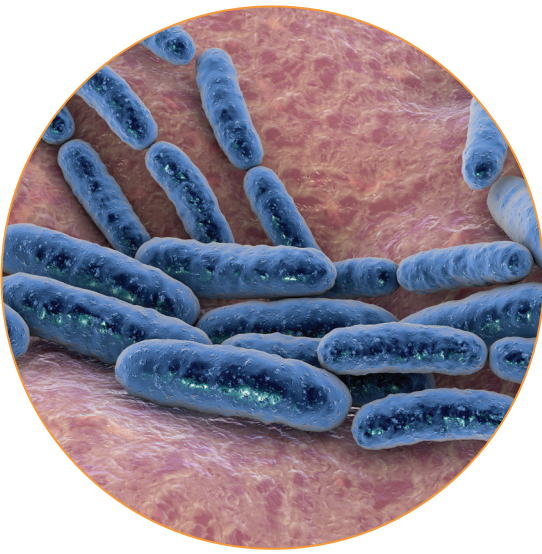
How Can Probiotics Influence Brain Function?

Gut Microbiome, Inflammation, and Stress Pathway

Probiotics promote mental flexibility and alleviate stress in humans, along with restoring gut microbiota and reversing stress-induced changes in our body.

The gut microbiome may communicate with the brain through neural and humoral pathways, while involving several neurotransmitters and signaling molecules. The immune response, especially inflammatory system, plays a critical role in the microbiome and in mental health. Thus, many studies were conducted to explore the beneficial effect of specific probiotic.

Significant, positive results were observed and some studies showed that the production of neurotransmitter-like metabolites by specific probiotic strain could be the possible mediator of gut-brain axis.



How do we make better choices? We trust science!

Self-Care truly means starting with digestive health

In the field of pharmacology, the microbiota-gut-brain axis is emerging as a particular area of interest and a potential new therapeutic target for effective treatment of nervous system disorders.

In parallel, consumer interest in the role of nutrition in overall health is expanding, with more people globally understanding there is a connection between their digestive health and overall good health.

Caring for one's self is an important way to manage the stress associated with our daily life, as well as an opportunity to make positive choices. As we are just beginning to understand the connection between digestive health, immune health, brain health and overall well-being, the choices we make can have a large impact on our overall health and well-being, mentally and/or physically.

As awareness of the value of maintaining a healthy microbiome has grown, so has our interest and demand for research supported probiotic ingredients that simplify our choices.

Nowadays, in these uncertain times, recognizing the research-backed probiotic and the strain efficacy to support our overall health is the most credible way to trust these choices.

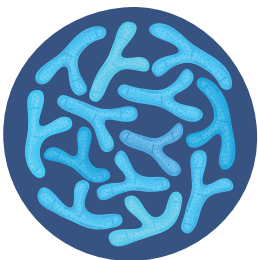
Microbiota-Gut-Brain Axis: Not All Strains Are Equal!

When it comes to Microbiota-gut-brain axis and our well-being, understanding the important distinctions between different probiotic strains and the substantial benefit is the key to differentiate. In a world of competing claims, it can be difficult for us to compare strains and choose the products best suited to our needs. In fact, more information about health in general and more information about the nutritional benefits of products are the key for clear choices.

Positive findings of one study looking at a particular strain and its impact on health cannot substantiate theories concerning the health benefits of another strain. Each Probiotic strain possess its own, distinct characteristics. Properties that may influence quality, safety, efficacy, benefits and the strain's suitability and/or stability over the time.

Probiotics is a catch-all term with strong consumer resonance, but a frequent misunderstanding is that all probiotic strains are the same. In the world of probiotics, strain differentiation is not just important, it's vital, because the benefits of a probiotic actually depend on the probiotic strain. Efficacy is strain-dependent, benefit claims need to be supported by data on strain-specific research.

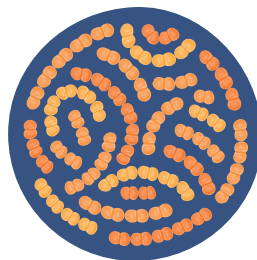
PROBIOTICS



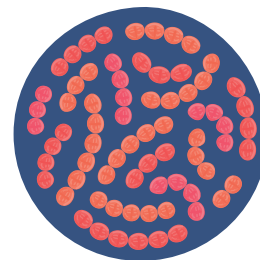
BIFIDO
BACTERIUM



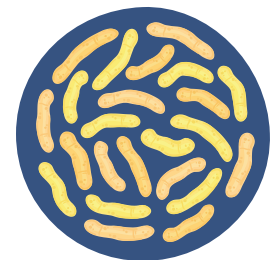
LACTO
BACILLUS



STREPTOCOCCUS
THERMOPHILUS



LACTO
COCCUS



PROPIONI
BACTERIUM

Plantarum DR7: Clinically Tested for GBA and Immune Support

Lactobacillus plantarum DR7

GENUS SPECIES STRAIN

What makes Plantarum DR7 stand out amongst other probiotic brands is simple:

Clinically Tested, Unique Mechanisms.

DR7 isn't just another probiotic. It is 100% naturally-sourced Lactobacillus plantarum. It is a clinically tested probiotic strain proven to help support Gut-Brain-Axis Benefits mood and immune health, while working around the clock to support the gastrointestinal health.

Broad Overview of DR7 Benefits

*Benefits beyond healthier Gut.**

Was developed from competent and reliable scientific research.

Has been studied in animals and humans.

*Supports the maintenance of a healthy mood and healthy levels of common and everyday stress and anxiety.**

*Probiotic strains optimized to support gut health and comfort.**

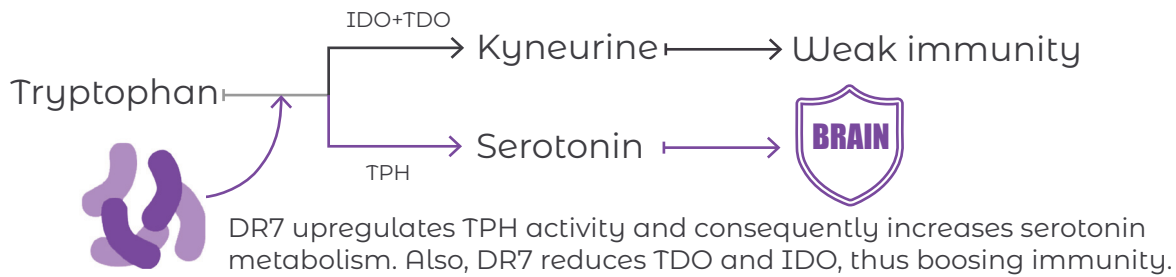
*Supports overall gastrointestinal health and maintenance of stress.**

Promotes brain health.

*Promotes health benefits along the gut-brain-axis.**

Like no other, has demonstrated its potential to exhibit positive health benefits on gut, brain and immunity.

So How Does Plantarum DR7 Work?



Beyond modulation of the gut microbiome and maintaining homeostasis,

L. plantarum DR7 enhances the serotonin pathway.

L. plantarum DR7 induces physiological changes which could be associated with changes in specific taxa of the gut microbiota along the serotonin and dopamine pathways.

Lactobacillus plantarum DR7 alleviates the symptoms of Upper Respiratory Tract Infection by improving inflammatory parameters and enhancing immunomodulatory properties.

Lactobacillus plantarum DR7 stimulates the Immune response.

Lactobacillus plantarum DR7 supports the body's reduction of inflammation and oxidative stress.

Lactobacillus plantarum DR7 supports and protects Upper Respiratory Health.

DR7 Mechanisms of Action

a) by the modulation of gastrointestinal microbial profile via suppressing gut pathogen populations and increasing the population of lactobacilli,

b) by decreasing pro-inflammatory cytokines and increasing anti-inflammatory cytokines in the plasma, and

c) by reducing inflammation in the lower intestines

d) by upregulating the tryptophan-serotonin pathway, driving the body's tryptophan pool away from the production of kynurenine, boosting immunity.

e) by reducing the plasma pro-inflammatory cytokines (TNF- α and IFN- γ).

f) by increasing plasma anti-inflammatory cytokine IL-10.

g) by decreasing the plasma peroxidation and oxidative stress levels due to inflammation.

f) by supporting the gut microbiome communication with immune cells to help manage how the body responds to a threat.



Human Clinical Studies and Plantarum DR7

Study 1 (Chong et al., Beneficial Microbes, 2019) Emphasis on Stress and Anxiety

Stress and anxiety disorders are two of the most common psychiatric disorder in our modern lifestyles, affecting both children and adults.

Memory & cognition are affected by stress and anxiety. Lactobacillus plantarum DR7 has proven to be used as a nutritional-based natural strategy to improve psychological functions, cognitive health and memory in stressed adults.

In 111 stressed adults (DR7 n=56, placebo n=55), the consumption of Lactobacillus plantarum DR7 (1×10^9 cfu/day) for 12 weeks better improved cognitive and memory functions in normal adults (>30 years old), such as basic attention, emotional cognition, and associate learning ($P < 0.05$), as compared to the placebo and young adults (<30 years old).

The administration of Lactobacillus plantarum DR7 enhanced the serotonin pathway, as observed by lowered expressions of plasma dopamine Beta-hydroxylase (DBH), tyrosine hydroxylase (TH), indoleamine 2,3-dioxygenase and tryptophan 2,3-dioxygenase accompanied by increased expressions of tryptophan hydroxylase-2 and 5-hydroxytryptamine receptor-6, while stabilising the dopamine pathway as observed via stabilized expressions of TH and DBH over 12 weeks as compared to the placebo ($P < 0.05$).

The consumption of Lactobacillus plantarum DR7 for 12 weeks reduced symptoms of stress ($P = 0.024$), anxiety ($P = 0.017$), and total psychological scores ($P = 0.022$) as early as 8 weeks among stressed adults compared to the placebo group as assessed by the DASS-42 questionnaire.

Human Clinical Studies and Plantarum DR7 (continued)

Study 2 (Liu et al., Beneficial Microbes, 2020) Emphasis on Neurotransmitter Pathways

In the study above it was reported that the administration of *Lactobacillus plantarum* DR7 for 12-weeks reduced stress and anxiety in stressed adults as compared to the placebo group, in association with changes along the brain neurotransmitters pathways of serotonin and dopamine-norepinephrine.

In the current study, the effects of DR7 on gut functions, gut microbiota compositional changes was evaluated, and the correlations between microbiota changes and the pathways of brain neurotransmitters was determined. In 124 moderately stressed adults (DR7 n=60, placebo n=60), the administration of (1×10^9 cfu/day) DR7 prevented an increase of defecation frequency over 12 weeks as compared to the placebo ($p=0.044$), modulating the increase of stress-induced bowel movement.

Over 12 weeks, alpha diversity of gut microbiota was higher in DR7 than the placebo group across class ($p=0.005$) and order ($p=0.018$) levels, while beta diversity differed between groups at class and order levels ($p<0.001$). Differences in specific bacterial groups were identified, showing consistency at different taxonomic levels that survived multiplicity correction.

The present data shows that physiological changes induced by *L. plantarum* DR7 could be associated with changes in specific taxa of the gut microbiota along the serotonin and dopamine pathways.

Study 3 (Chong et al., Journal of Dairy Science, 2019)

Lactobacillus plantarum DR7 alleviated the symptoms of URTI by improving inflammatory parameters and enhancing immunomodulatory properties.

In 109 adults (DR7, n = 56; placebo, n = 53), *Lactobacillus plantarum* DR7 reduced the duration of nasal symptoms and frequency of upper respiratory tract infections compared with the placebo over an administration period of 12-weeks. This was accompanied by reduced plasma inflammatory and oxidative stress levels in the DR7 group as compared to the placebo. The mechanisms involve enhanced plasma anti-oxidative properties, promotion of mucosal barrier integrity and activation of NK cells which are involved in innate immunity.

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