Technical Report

Significance of *Lactobacillus casei* in CanXida Restore (Formula RST)

*"In CanXida Restore (Formula RST), **Lactobacillus casei** plays a central role in promoting gut health, inhibiting pathogens, and defending against Candida overgrowth, supporting overall well-being and immune health.*

Contents

Executive Summary

Lactobacillus casei is a versatile probiotic well-known for its significant functional properties and health. Its functional properties encompass antimicrobial substance production, gut barrier enhancement, pathogen adhesion reduction, immune system modulation, survival in the digestive system, trophic effects, tight-junction gene expression, and antioxidant effects. The extensive health benefits of *Lactobacillus casei* span from microbial balance restoration and improved digestion to modulate immune function, vaginal health promotion, allergy reduction, and broader health advantages.

Designated as Generally Recognized as Safe (GRAS) by the FDA, *Lactobacillus casei* showcases efficacy against a spectrum of pathogens, including Candida albicans.
In CanXida Restore Formula, *Lactobacillus casei* plays a central role by balancing gut microbiota, inhibiting pathogens, and supporting gut and immune health*.

* *These statements have not been evaluated by Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.*

1. Introduction

Lactobacillus casei is a member of the Lactobacillus genus, which consists of many different species. Since April 2020, *L. casei* has undergone an official reclassification and is now known as *Lacticaseibacillus casei* (Zheng et al., 2020).

Among the most researched species is *Lactobacillus casei* on account of its potential in the industrial, commercial, and applied health sectors. It is commonly found in various functional foods. This bacterium has been identified as a type of bacteria that can survive with or without oxygen, can tolerate acidic conditions, and does not form spores. Found in the reproductive and digestive tracts of the human body, this species is a rod-shaped, gram-positive microorganism devoid of spores (Oozeer et al., 2006; Zheng et al., 2020).

It is often present in dairy products as a nonstarter lactic acid bacterium (LAB). This bacterium is known for its ability to tolerate a broad variety of pH levels and temperatures. It may be found in Sicilian green olives and maturing cheddar cheese (Lorenzo et al., 2018).

There have been reports on the effectiveness of various strains of *L. casei*, including BL23, ATCC 393, and Shirota, in alleviating intestinal diseases. These strains have shown to enhance the Disease Activity Index score, restore histopathological damage, and inhibit the expression of pro-inflammatory cytokines and NF-κB signaling. These results suggest that some strains of *L. casei* may help with gastrointestinal disorders (Liu et al., 2021)

2. Functional Properties of *Lactobacillus casei*:

Lactobacillus casei possesses numerous functional properties that make it a promising probiotic with potential benefits *.

2.1. Production of antimicrobial substances:

The presence of antimicrobial substances such as organic acids and bacteriocins hinders the development of harmful microbes. *Lactobacillus casei* has antimicrobial efficacy against both gram-positive and gram-negative pathogenic bacteria, including those that are resistant to antibiotics. This capacity promotes the proliferation of beneficial microorganisms and helps to maintain a

balanced and healthy gut environment (Ullah et al., 2017).

2.2. Enhancement of gut barrier function:

Lactobacillus casei has been found to effectively protect the integrity of intestinal epithelial cells, preventing any impairment in their barrier function. The precise mechanism by which probiotics impact epithelial barrier function remains unclear. However, it was observed that when gut cells were pre-treated with *L. casei* before undergoing induced cytokine dysfunction, a protective effect was observed (Eun et al., 2011).

2.3. Reduces Pathogen Adhesion:

Lactobacillus casei has the capacity to inhibit pathogen adherence. This probiotic prevents dangerous microorganisms from attaching to human surfaces by using methods such as competitive exclusion or interference. This decrease in pathogen adherence is an important component of *L. casei*'s capacity to promote gastrointestinal health by avoiding the colonization of harmful bacteria (Iqbal et al., 2021; Lee & Puong, 2002).

2.4. Modulation of the immune system:

Certain strains of *L. casei* have exhibited the capacity to modify the composition of the gastrointestinal tract and stimulate the innate immune system in humans. For immune support, *L. casei* DN-114001 has undergone extensive testing, and *L. casei* Shirota has been demonstrated to stimulate natural killer cells, which target numerous types of infectious cells (Liu et al., 2020; Min et al., 2023; Reale et al., 2012).

2.5. Survival and Colonization:

Lactobacillus casei demonstrates persistent in traveling the digestive system, surviving acidic conditions in the stomach, and reaching the intestine. Its ability to cling to intestinal epithelial cells suggests the possibility of colonization, which is critical for probiotic effectiveness (Oozeer et al., 2006).

2.6. Trophic Effects:

The presence of *L. casei* has a positive impact on the visual characteristics of enterocytes, suggesting that it may have effects beyond the gastrointestinal tract (Bertazzoni Minelli et al., 2004). This impact on cellular growth and

maintenance plays a role in the overall well-being of the gastrointestinal system.

2.7. EPS Production:

Lactobacillus casei produces exopolysaccharides (EPS) that provide protection for the bacteria within the digestive system. This characteristic enhances its capacity to navigate and tolerate the challenges of the gastrointestinal tract (Hill et al., 2018; Yang et al., 2023).

2.8. Expression of Tight-Junction Genes:

Prolonged fermentation of *L. casei* results in enhanced gene expression related to tight junctions. This implies a function in preserving the integrity of the intestinal barrier, which is essential for avoiding diseases such as intestinal leaky diseases (Jung et al., 2021).

2.9. Antioxidant effect:

The antioxidant effects of *L. casei* are an area of ongoing research. Current studies suggest that these bacteria may contribute to antioxidant activity through the production of compounds and the induction of host antioxidant enzymes (Kleniewska et al., 2016; Wang et al., 2021). However, additional research is needed to establish the precise antioxidant potential of *L. casei* and its implications for health.

3. Health Benefits of *Lactobacillus casei:*

Lactobacillus casei is lactic acid bacterium. It is found in the gastrointestinal system and fermented foods like yogurt and probiotic supplements. *L. casei* may have health advantages, however probiotic reactions vary.

3.1. Restoring Microbial Balance:

Dysbiosis refers to an imbalance in the delicate ecosystem of microorganisms that reside within your body, particularly in the gut. This imbalance can lead to a wide range of chronic problems. *L. casei* aids in restoring a balanced gut microbiota by promoting the growth of beneficial bacteria and inhibiting harmful ones (Manouni el Hassani et al., 2019; Olvera-Rosales et al., 2021; Qin et al., 2022).

Table 1: Clinical trials that have used *Lactobacillus casei* for either treatment or prevention are detailed here. *Source: clinicaltrials.gov*

Clinical trial ID	Health Condition	Status
NCT00822328	Signs and Symptoms, Digestive	*Completed*
NCT03605108	• Gut Microbiome • Gut Lipidome • Blood Lipidome • Skin Microbiome • Skin Lipidome	*Completed*
NCT02151825	• Gut Microbiota • Adiposity	*Completed*
NCT04841694	Human Microbiome	*Completed*
NCT05812820	Diarrhea	*Active, Not Recruiting*
NCT01837472	Irritable Bowel Syndrome	*Completed*
NCT04954846	• Dysbiosis • Stroke, Ischemic	*Recruiting*
NCT05750433	4. Gastrointestinal Dysfunction	*Active, Not Recruiting*
NCT05836155	Dysbiosis	*Recruiting*
NCT04985877	• Aging • Inflammation • Sarcopenia	*Unknown Status*

NCT03923985	Vaginal Flora	*Completed*
NCT02979288	Lactobacillus Infection	*Completed*
NCT06124313	• Vaginal Health • Irritable Bowel Syndrome	*Active, Not Recruiting*
NCT01160796	Bacterial Vaginosis	*Completed*
NCT06165354	Vaginitis	*Not Yet Recruiting*
NCT04997187	Constipation - Functional	*Completed*
NCT01161784	Constipation	*Completed*

4.1. Improved Digestion:

Lactobacillus casei can help alleviate symptoms of digestive diseases, such as

- **Constipation**

Lactobacillus casei may aid constipation by promoting regular bowel habits and improving intestinal motility (Sakai et al., 2015).

- **Diarrhea**

Lactobacillus casei has been associated with the reduction of diarrhea symptoms, potentially by restoring gut microbial balance (Lai et al., 2019; Ren et al., 2022).

- **Irritable Bowel Syndrome (IBS):**

Lactobacillus casei may contribute to the management of IBS symptoms, including abdominal discomfort and irregular bowel movements * (Compare et al., 2017; Hou et al., 2020; Thijssen et al., 2016).

- **Inflammatory Bowel Disease (IBD):**

Lactobacillus casei shows promise in mitigating inflammation associated with IBD,

potentially aiding in the modulation of disease severity (Liu et al., 2021).

4.2. Enhanced immune function:

Lactobacillus casei may strengthen your immune system, making you less susceptible to infections and illnesses (Mazziotta et al., 2023; Slykerman et al., 2022).

4.3. Improved Vaginal Health:

Lactobacillus casei contributes significantly to enhancing vaginal health by preventing and treating vaginosis, as well as restoring the natural balance of the vaginal microbiota (Paniágua et al., 2021; Petricevic et al., 2023).

4.4. Reducing Allergies

Lactobacillus casei demonstrates a potential role in reducing allergies by modulating the immune response and promoting immune tolerance, which may contribute to a decreased susceptibility to allergic reactions (Schiffer et al., 2011; Steiner & Lorentz, 2021).

4.5. Other Health Benefits

Lactobacillus casei offers broad health benefits beyond digestion (Imran et al., 2015; Kato-Kataoka et al., 2016; Kim et al., 2015; Kumar et al., 2013; Sáez-Lara et al., 2016). It may promote skin health by maintaining a balanced microbiome, contribute to oral health by inhibiting harmful bacteria, and show promise in cardiovascular well-being by potentially managing cholesterol levels. These varied effects highlight the versatile impact of *L. casei* on overall health. It has also shown potential in treating stress and diabetes.

5. Biosafety Profile of *Lactobacillus casei*

Lactobacillus casei, a Gram-positive bacteria found in the human gastrointestinal tract, has been designated Generally Recognized as Safe (GRAS) by the United States Food and Drug Administration (FDA) (Hill et al., 2018). Its GRAS status emphasizes its safety for human consumption, encouraging its use in probiotic supplements.

Lactobacillus casei has also been investigated for therapeutic use by **DRUG BANK** under accession ID **DB16541**

Not only is it a natural component of the microbiota, residing mostly in the digestive

tract, but it also plays an important role in the manufacture of fermented foods such as yogurt and certain cheeses. Its presence in a variety of natural fruits and vegetables further ensures its safety* (Jung et al., 2021).

Despite its generally positive profile, caution is advised, particularly for individuals with compromised immune systems, as they may be susceptible to infections or complications (Guzek et al., 2023).

6. Effective Targets of *Lactobacillus casei:*

Lactobacillus casei demonstrates antimicrobial properties through various mechanisms, such as competitive exclusion, organic acid production, and immune system modulation (Divyashree et al., 2021; el Manouni el Hassani et al., 2019; Enany & Abdalla, 2015; Mirnejad et al., 2013; Paniágua et al., 2021).

- Among the ***pathogens*** (bad bacteria), *L. casei* is effective against*

6.1. *Escherichia coli* (Pathogenic Strains):

Escherichia coli is responsible for causing foodborne illnesses, which can result in various gut-related symptoms including diarrhea, and abdominal cramps.

6.2. *Clostridium difficile*:

Clostridium difficile can cause colitis, especially following antibiotic treatment, leading to intense diarrhea and potentially life-threatening complications.

6.3. *Salmonella Species*:

Salmonella species have a significant impact on human health, as they are responsible for causing salmonellosis. This condition manifests with various symptoms such as diarrhea, fever, abdominal cramps, and vomiting.

6.4. *Helicobacter pylori*:

It colonizes the stomach lining, causing persistent gastritis, and peptic ulcers.

6.5. *Shigella*:

Shigella is responsible for causing shigellosis, a bacterial infection that spreads easily and

leads to symptoms such as diarrhea, abdominal cramps, fever, and nausea.

6.6. *Enterobacteriaceae*:

The *Enterobacteriaceae* family consists of pathogenic bacteria, such as *Klebsiella* and *Enterobacter*, which are responsible for a range of infections, including urinary tract infections.

6.7. *Staphylococcus*:

Staphylococcus species can cause a range of infections to severe conditions like pneumonia, bloodstream infections, and toxic shock syndrome.

6.8. *Clostridium perfringens*:

It is possible for it to cause food poisoning, which can lead to cramping in the abdominal region and diarrhea.

- Among the ***fungal pathogens*** *L. casei* is effective against*

6.9. Candida albicans:

Causes infections such as oral thrush and vaginal yeast infections. Overgrowth can lead to candidiasis, with symptoms depending on the affected area.

7. Significance of *Lactobacillus casei* in CanXida Restore Formula

In the formulation of CanXida Restore, *L. casei* plays a central role in fostering a balanced gut microbiota and contributing to overall gastrointestinal and immune health*.

Its versatile functional properties, including the production of antimicrobial substances and the inhibition of pathogen adherence, actively work to create an environment conducive to the growth of beneficial bacteria*.

This probiotic not only acts as a defender against harmful pathogens but also enhances gut barrier function, protecting the integrity of intestinal epithelial cells. Thus, *L. casei* acting as a preventive measure against the translocation of Candida and reducing the risk of associated health concerns*.

Beyond its functional properties, the health benefits of *L. casei* further underscore its significance in Candida restoration. From modulating the immune system to promoting digestive well-being, *L. casei* contributes holistically to the formula's goal of combating Candida overgrowth and supporting overall health*.

In summary, within the Candida Restore formula, *L. casei's* functional properties and health benefits synergize to create a comprehensive approach. By defending against pathogens, enhancing gut barrier function, and promoting overall well-being, *L. casei* plays a vital role in restoring balance and fostering a healthy environment, essential for addressing Candida concerns*.

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