Technical Report

Significance of *Bifidobacterium longum* in CanXida Restore (Formula RST)

"In CanXida Restore (Formula RST), **Bifidobacterium longum** plays a crucial role by leveraging its antimicrobial, immune-modulating, and detoxification capabilities to support gut health, manage Candida overgrowth, and enhance overall well-being."

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Executive Summary

Bifidobacterium longum, a Gram-positive bacterium residing in the human gastrointestinal tract, is recognized for its vital role in the gut microbiota, especially in infants. This probiotic specie has been extensively studied for its health benefits. The functional properties of *B. longum* encompass crucial aspects such as enhancing gut barrier function, fermenting non-digestible carbohydrates, immunomodulation, anti-inflammatory properties, antimicrobial activity, vitamin production, and adaptation to stress conditions. These properties contribute to its association with health benefits, including gastrointestinal health, colitis symptom alleviation, metabolic health, allergy prevention, immune system improvement, and detoxification.

Recognized as Generally Recognized as Safe (GRAS), *B. longum's* low infection risk and adaptability in stressful conditions make it a valuable probiotic. Its role in reducing harmful bacteria, its efficacy in clinical trials, and its synergistic interactions emphasize its significance in the CanXida Restore formula for holistic gut support and Candida management*.

^{*} 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

Bifidobacterium longum is a non-motile, anaerobic, non-spore forming rod-shaped **Gram-positive** bacteria commensal organism found in the gastrointestinal tract (Freitas & Hill, 2018).

It is considered an important member of the human gut microbiota and is particularly prevalent in the gut of infants. It has a wide range of health benefits. These vary from the generation of bioactive compounds to the interaction of bifidobacterial surface-associated chemicals with the host (Zhang, Yu, Zhao, Zhang, & ..., 2019).

The *Bifidobacterium longum* species consists of three subspecies:

- longum
- infantis
- suis

These strains have been extensively studied and utilized as **probiotics**, specifically designed for use in both children and adults (Quigley, 2017).

According to definition established by FAO/WHO:

Probiotics are the "Live microorganisms that, when administered in adequate amounts, confer a health benefit to the host"

Research has shown that *B. longum*, either on its own or in combination with other strains and prebiotics, can have a positive impact on different body systems. This suggests that *B. longum* may help alleviate disease symptoms and potentially prevent the development of illnesses. These findings highlight the potential role of *B. longum* in the prevention and management of various diseases, starting from early life and continuing throughout the human lifespan (Mills et al., 2023a).

2. Functional Properties of *Bifidobacterium longum*:

Bifidobacterium longum, a probiotic bacterium, has many functional features that contribute to its potential health advantages, include:

2.1. Enhancement of gut barrier function:

Bifidobacterium longum, has been associated with the enhancement of gut barrier function. Research suggests that *B. longum* plays a pivotal role in promoting the integrity of the intestinal barrier, contributing to the prevention of leaky gut syndrome and encouraging the body's defense against harmful pathogens. By fortifying the gut barrier, *B. longum* supports a healthier and more resilient gastrointestinal environment (Abdulqadir et al., 2023).

2.2. Fermentation of Non-Digestible Carbohydrates:

Bifidobacterium longum has the ability to ferment non-digestible carbohydrates, such as dietary fiber and resistant starch.

Fermentation results in the production of short-chain fatty acids, specifically acetate, which play a crucial role in promoting gut health and preserving the integrity of the intestinal barrier (Fukuda et al., 2011; Silva et al., 2020).

2.3. Immunomodulation:

Bifidobacterium longum has immunomodulatory effects, influencing both innate and adaptive immune responses. It can stimulate the production of certain antibodies and cytokines, promoting a balanced immune response and potentially enhancing resistance to infections (Dong et al., 2022).

2.4. Anti-Inflammatory Properties:

Bifidobacterium longum lowers inflammation by modulating immune system stability, enhancing intestinal barrier integrity, and improving acetate synthesis (Chichlowski et al., 2020).

This anti-inflammatory activity may contribute to its potential protective effects against inflammatory bowel diseases and other conditions associated with chronic inflammation*.

2.5. Antimicrobial Activity:

B. longum produces antimicrobial compounds, such as bacteriocins, which can inhibit the growth of pathogenic bacteria (Inturri et al., 2019a).

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This antimicrobial activity contributes to the maintenance of a healthy microbial balance in the gut.

2.6. Vitamin Production:

Some strains of *B. longum* are capable of producing essential vitamins such as riboflavin (vitamin B2), pyridoxine (vitamin B6), cobalamin (vitamin B12), and ascorbic acid (vitamin C) (Ghoddusi & Tamime, 2014).

The production of vitamins by *B. longum* may contribute to the overall nutritional status of the host.

2.7. Adaptation to Stress Conditions:

B. longum possesses various mechanisms that enable it to adapt to stressful environmental conditions, thereby improving its chances of survival and optimizing its functionality within the gastrointestinal tract (Ghoddusi & Tamime, 2014; Sánchez et al., 2013).

3. Health Benefits of *Bifidobacterium longum*

Bifidobacterium longum, a probiotic bacterium, has been associated with several health benefits. While the extent of these benefits may vary among strains, research suggests that *B. longum* can contribute to overall well-being in the following ways:

3.1. Gastrointestinal Health:

Bifidobacterium longum is well-known for its beneficial effects on gastrointestinal health (Mills et al., 2023) i.e.,

- IBS- Irritable Bowel Syndrome
- IBD- Inflammatory Bowel Disease
- Constipation
- Diarrhea

3.2. Management of Colitis Symptoms

Bifidobacterium longum, a prevalent gut microbiota member, protects the intestinal barrier and maintains tissue structure. Its abundance helps balance the gut microbiota, offering relief from colitis symptoms. By fostering a healthy microbial community and supporting intestinal integrity, *B. longum* plays a crucial role in managing inflammation associated with colitis (W. Kim et al., 2018).

3.3. Metabolic Health:

Research suggests that *B. longum* may have metabolic benefits, including the modulation of lipid metabolism and blood glucose levels.

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

Clinical trial ID	Health Condition	Status
NCT05054309	IBS - irritable bowel syndrome	Recruiting
NCT05086458	Gut Microbiota	Unknown status
NCT01650753	Bacterium; Agent	Completed
NCT05286047	Atopic Dermatitis	Recruiting
NCT00803829	Ulcerative Colitis	Completed
NCT03994315	Infant Gut Microbiome	Completed
NCT03815617	Irritable Bowel Syndrome	Completed
NCT05339243	Irritable Bowel Syndrome with Diarrhea	Completed
NCT02566876	Dyspepsia ChronicIrritable Bowel Syndrome	Completed
NCT03388112	Gastrointestinal Microbiome	Unknown status
NCT03704727	 Intestinal Permeability Gastrointestinal Irritation Mucositis 	Completed

NCT04997057	Irritable Bowel Syndrome with Constipation	Completed
NCT03530501	Inflammation	Completed
NCT02756221	Gastroenteritis	Completed
NCT01887834	 Colitis, Mucous Colon, Irritable Colonic Diseases, Functional Digestive System Diseases Irritable Bowel Syndrome 	Completed

3.4. Allergy Management:

Studies have investigated the ability of *B. longum* to regulate allergic reactions, indicating it's potential in preventing or managing allergies (Niu et al., 2023).

3.5. Improving immunity:

Research indicates that *B. longum* has a significant impact on the immune system, improving the body's ability to combat harmful pathogens. *B. longum* plays a significant role in improving the immune systems of older individuals, making it

particularly valuable for the elderly (Akatsu et al., 2013).

3.6. Detoxification:

Bifidobacterium longum has been extensively studied for its capacity to effectively bind and detoxify specific harmful substances, thereby aiding in the elimination of toxins from the body (Pop et al., 2022).

3.7. Management of Dysbiosis:

Dysbiosis, an imbalance in gut bacteria, can lead to health issues. *B. longum* aids gut health by promoting balance through fermentation and anti-inflammatory properties. Using probiotics or fermented foods with *B. longum* may help improving dysbiosis symptoms* (Dixit et al., 2021; Wong et al., 2019; Zhou et al., 2020).

Individual responses to probiotics can vary, and the overall effectiveness may depend on factors such as the specific health condition, the host's microbiota, and lifestyle factors. It is recommended to seek guidance from a physician prior to integrating probiotics, such as *B. longum*, into one's treatment or supplementation, particularly for those who have pre-existing health conditions.

4. Biosafety Profile of *Bifidobacterium longum*

Bifidobacterium longum, probiotic а bacterium, exhibits a generally favorable biosafety profile, positioning it as a safe and beneficial component of the human microbiota. Acknowledged as Generally Recognized as Safe (GRAS) by regulatory authorities, including the U.S. Food and Drug Administration, B. longum is a natural inhabitant of the gastrointestinal tract, emphasizing its historical association with the human host (Zhang, Yu, Zhao, Zhang, Zhai, et al., 2019).

Also, *B. longum* presents low risk of infection in healthy persons due to its non-pathogenic nature and the absence of virulence factors*. The bacterium's ability to adapt to the gastrointestinal environment, including exposure to stomach acid and bile salts, is crucial for its functionality as a probiotic.

Bifidobacterium longum infantis and Bifidobacterium longum Infantis 35624, examined under DRUGBANK accession IDs DB14222 and DB17871, are both associated with a favorable safety profile, reinforcing their suitability for therapeutic or healthrelated applications.

Furthermore, *B. longum* exhibited a favorable safety profile by not producing ammonia or biogenic amines like histamine, cadaverine, or tyramine. It showed trace amounts of putrescine, comparable to or lower than levels found in commonly consumed foods. *B. longum* demonstrated neither hemolytic nor mucin-degrading activity, underscoring its safety for eating (M. J. Kim et al., 2018).

Clinical trials and studies on *B. longum* supplementation have reported a good safety profile, with mild and transient adverse

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effects typically limited to gastrointestinal symptoms*. While generally considered safe, caution is advised for vulnerable populations with compromised immune systems*.

5. Effective Targets of *Bifidobacterium longum*

Bifidobacterium longum has been associated with reducing the abundance of some potentially harmful bacterial genera (Inturri et al., 2019b; Lim & Shin, 2020; Mills et al., 2023c; Silva et al., 2020). Here are some examples:

Clostridium:

Bifidobacterium longum has been studied for its potential to inhibit the growth of certain *Clostridium* species, which can include pathogenic strains.

Escherichia Coli:

Some research suggests that *B. longum* may have positive effects against certain pathogenic strains of *Escherichia coli*.

Salmonella:

Although the nature of interactions may differ, some studies have investigated the capacity of *B. longum* to potentially decrease

the colonization of *Salmonella*, which is a prevalent disease transmitted by food.

Helicobacter:

Research has been conducted on *B. longum* to explore its ability to regulate the gut environment and decrease the presence of *Helicobacter pylori*, a bacterium linked to stomach ulcers.

Candida:

Bifidobacterium longum, a beneficial probiotic, is associated with the prevention of the overgrowth of organisms like *Candida*.

6. Significance of *Bifidobacterium longum* in CanXida Restore Formula

Bifidobacterium longum inclusion in CanXida Restore formula can be particularly beneficial due to its multifaceted approach to supporting gut health and potentially mitigating Candida overgrowth.

B. longum strengthens the intestinal barrier, preventing leaky gut and protecting against harmful pathogens. This improved barrier can hinder Candida's ability to penetrate the gut

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lining and potentially cause systemic infections*.

B. longum's antimicrobial properties, immune modulation, and detoxification capabilities make it a valuable tool in CanXida Restore for controlling Candida overgrowth, reducing inflammation, and managing associated symptoms*.

B. longum's various health benefits, including improved digestion, nutrient absorption, and reduced inflammation, create a more favorable environment for overall gut health. This can indirectly contribute to managing Candida overgrowth by promoting a thriving community of beneficial gut bacteria*.

B. longum is usually considered safe and well tolerated, making it a viable probiotic option

for treating Candida. Furthermore, its synergistic interactions with other substances in the CanXida Restore mix have the potential to improve its efficacy in controlling Candida and supporting gut health*.

In conclusion, B. longum's inclusion in CanXida Restore formula holds promise for its multi-pronged approach to gut health and potential Candida management. Its ability to strengthen the gut barrier, produce antimicrobials, modulate immunity, and detoxify, alongside its general gut-supporting properties, can contribute to a more balanced and resilient gut environment, potentially aiding in controlling Candida overgrowth and promoting overall health*.

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