Technical Report

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

"*CanXida Restore Formula (RST) utilizes* ***Bifidobacterium bifidum*** *as a comprehensive solution for overall gut health, addressing microbial balance, inflammatory conditions, and pathogens.****"***

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Executive Summary

Bifidobacterium bifidum, a naturally occurring probiotic found in the gut, boasts a wide range of health benefits. It colonizes the intestines, fostering a balanced microbiome, and produces lactic acid to create an unfavorable environment for harmful bacteria. This remarkable probiotic also modulates the immune system, potentially enhancing defenses and reducing inflammation, and exhibits antimicrobial activity against pathogens like Candida. *B. bifidum* has also potential to alleviate various digestive disorders, including diarrhea, constipation, acid-related dyspepsia, and inflammatory bowel diseases.

Furthermore, *B. bifidum*, is acknowledged as Generally Recognized as Safe (GRAS), and is widely utilized in probiotic supplements, and commonly found in various fermented products. In CanXida Restore Formula, *B. bifidum* is strategically utilized to promote a balanced microbiome, alleviate digestive concerns, and pathogens growth i.e. Candida*.

1. Introduction

Bifidobacterium bifidum is a Bifidobacterium genus bacterial species. Bifidobacteria are bacteria that have a branched, rod-shaped structure. They are immobile, do not form spores, and are Gram-positive, anaerobic, and catalase-negative. Bifidobacteria are a part of *Bifidobacteriaceae* family and the phylum *Actinobacteria*. There are currently more than 90 species in the Bifidobacterium genus (Chen et al., 2021).

More than 80% of the microorganisms in the colon are Bifidobacteria, with *B. bifidum* being the second most common species in breastfed newborns. The amounts of Bifidobacteria drop significantly during adulthood but stay largely constant 2–14% until they begin to decline further in older age (Arboleya et al., 2016; Ku et al., 2016).

Bifidobacteria, particularly *B. bifidum*, are essential for gut health. They inhibit harmful microbes, potentially reducing IBS symptoms, diarrhea, and infections. Lower Bifidobacteria levels correlate with conditions like obesity and diabetes. Probiotics, including *B. bifidum*, support the immune system and may prevent pathogen growth (Arboleya et al., 2016; Ku et al., 2016).

B. bifidum is frequently utilized as a probiotic supplement due to its beneficial properties. It is commonly found in commercial probiotic products that are designed to enhance digestive health, modulates the immune system, and improve overall health (Chen et al., 2021; Das et al., 2022).

According to FAO/WHO:

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

Furthermore, researchers are currently investigating the potential therapeutic uses of *B. bifidum* in a range of health conditions, particularly gastrointestinal disorders.

2. Functional Properties of *Bifidobacteria bifidum*:

Bifidobacterium bifidum, like other probiotic bacteria, has a variety of functional characteristics that contribute to its health-promoting effects. Here are some of *B. bifidum's* important functional properties:

2.1. Adhesion and Colonization:

Bifidobacterium bifidum thrives within our colon, promoting a healthy gut balance. They stick to gut walls, aiding their colonization and crucial interactions with our body through different lipoproteins and mucin binding abilities (González-Rodríguez et al., 2013).

2.2. Production of Metabolites:

Bifidobacteria are lactic acid-producing bacteria (Pokusaeva et al., 2011), leading to a decrease in the pH of the gut environment. This acidification can create an inhospitable environment for pathogenic bacteria while promoting the growth of other beneficial bacteria (Saez-Lara et al., 2015).

2.3. Immune Modulation:

Bifidobacterium bifidum has been associated with the modulation of the immune system. It potentially enhances the body's defense mechanisms, by (Gavzy et al., 2023)

- By decreasing pro-inflammatory cytokine synthesis*
- By supporting in the production anti-inflammatory cytokine*

2.4. Antimicrobial Activity:

Some strains of *Bifidobacterium bifidum* are known to produce antimicrobial substances, such as bacteriocins (bifidocin B), which can inhibit the growth of pathogenic bacteria in the gut (Collado et al., 2005).

By utilizing available nutrients and producing antimicrobial substances, *B. bifidum* can compete with and inhibit the growth of pathogenic microorganisms in the gut. For instance, a clinical trial was conducted with 79 individuals who were infected with *H. pylori*. The results showed that *B. bifidum* had a positive impact on both upper gastrointestinal and overall symptoms (Miki et al., 2007).

2.5. Antioxidant Properties:

Studies suggest that *Bifidobacterium bifidum* can scavenge free radicals, produce antioxidant compounds, and contribute to a reduction in oxidative stress (Hoffmann et al., 2021; Kim et al., 2020). Its anti-inflammatory effects may further indirectly support antioxidant activity by mitigating inflammation-induced oxidative stress. While research is still ongoing.

3. Health Benefits of *Bifidobacteria bifidum:*

Bifidobacterium bifidum, a beneficial strain of probiotic, has numerous potential health advantages, proved by scientific investigation.

Following are the some of the health benefits of the *B. bifidum:*

3.1. Restoring Normal Bowel Bacterial Flora

Bifidobacterium bifidum plays a crucial role as a probiotic in restoring a harmonious equilibrium within the gut microbiota. Its ability to attach to mucosal surfaces and colonize the gastrointestinal tract is crucial for maintaining a healthy and balanced microbial ecosystem (González-Rodríguez et al., 2013; Tojo et al., 2014).

3.2. Alleviation of Digestive Disorders:

Bifidobacterium bifidum, studied extensively, has shown potential in addressing gastrointestinal disorders (Gomi et al., 2015; URITA et al., 2015), such as

- Acid-related dyspepsia
- Diarrhea
- Abdominal pain
- Constipation
- Gastric

3.3. Management of Inflammatory Bowel Diseases:

Bifidobacterium bifidum exhibits promising properties in the management of Inflammatory Bowel Disease. Studies suggest that it can help reduce inflammation, and modulate the production of pro-inflammatory cytokines, contributing to a potential therapeutic approach for conditions like ulcerative colitis (Grimm et al., 2015; Palumbo et al., 2016).

3.4. Management of Inflammatory Bowel Syndrome:

Bifidobacterium bifidum demonstrates a potential role in managing irritable bowel syndrome. It may help alleviate symptoms such as pain, discomfort, bloating, and digestive disorders, contributing to improved gastrointestinal health (Terra et al., 2023).

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

Clinical trial ID	Health Condition	Status
NCT03877458	Infantile Colic	*Completed*
NCT02872675	• Asthma • Exercised Induced Asthma	*Completed*
NCT04035616	• Aging • Constipation • Multi-Core Disease	*Completed*
NCT04223479	• Ulcerative Colitis	*Completed*
NCT00540033	• Enterocolitis • Necrotizing	*Completed*
NCT01662206	Healthy	*Completed*
NCT01641341	Irritable Bowel Syndrome	*Completed*
NCT04958460	• Gut Microbiota • ADHD • Clinical Trial • Probiotics • Psychiatry	*Completed*
NCT01176227	• Colitis, Mucous • Colon, Irritable • Colonic Diseases, Functional • Digestive System Diseases • Irritable Bowel Syndrome	*Completed*
NCT04642482	• Insulin Resistance • Obesity	*Completed*
NCT05819281	Irritable Bowel Syndrome	*Recruiting*

NCT03959722	Gastrointestinal Symptoms	*Completed*
NCT04954846	• Dysbiosis • Stroke, Ischemic	*Recruiting*
NCT01667627	IBS	*Completed*
NCT05013060	Irritable Bowel Syndrome	*Unknown status*
NCT03704727	• Intestinal Permeability • Gastrointestinal Irritation • Mucositis	*Completed*
NCT02795845	Bacterial Vaginosis and Vaginal Candidiasis at Pregnancy	*Completed*
NCT00282113	• Growth • Premature Infants • Stool Bacterial Composition	*Completed*

3.5. Treating Acute Diarrhea:

In cases of acute diarrhea, *Bifidobacterium bifidum* has shown efficacy in various clinical trials. Its inclusion in probiotic formulations has been associated with preventing and reducing the duration of diarrhea episodes, showcasing its role in promoting digestive health during acute conditions.

3.6. Immune Function:

Bifidobacterium bifidum exhibits immune-modulating properties. Studies on stressed students, elderly individuals, and children with HIV indicate that supplementation enhances immune response, leading to increased healthy days* (Langkamp-Henken et al., 2015).

3.7. Others

Bifidobacterium bifidum offers diverse health benefits:

- Potential relief for seasonal allergy symptoms, particularly in respiratory and eye conditions (Dennis-Wall et al., 2017).

- Acts preventively and therapeutically, reducing the development of eczema (Sun et al., 2021).
- Demonstrates efficacy in controlling blood sugar and insulin levels (Sabico et al., 2017).
- Positive impact on blood fat profiles, improving *good cholesterol* and reducing triglycerides and *bad cholesterol*, offering cardiovascular benefits (Famouri et al., 2017; Moroti et al., 2012).

4. Effective Targets of *Bifidobacteria bifidum*

Following are some effective microbial targets of *Bifidobacterium bifidum* (Cong et al., 2023; Mahmoudi et al., 2013; Ricci et al., 2022):

❖ *Escherichia coli (E. coli):*

While some strains of *E. coli* are harmless and even beneficial, certain pathogenic strains can cause gastrointestinal infections, such as diarrhea, abdominal pain, and, in severe cases, more serious complications.

❖ *Salmonella:*

Salmonella infections can result in salmonellosis, characterized by symptoms like diarrhea, nausea, vomiting, abdominal cramps, and fever.

❖ *Clostridium difficile:*

Clostridium difficile infection (CDI) can cause antibiotic-associated diarrhea.

❖ *Helicobacter pylori:*

H. pylori is associated with gastritis and peptic ulcers. The bacterium can affect the stomach lining, leading to inflammation and contributing to the development of gastrointestinal conditions.

❖ *Staphylococcus aureus:*

S. aureus can produce toxins that, when ingested, may cause food poisoning. Symptoms include nausea, vomiting, abdominal cramps, and diarrhea. *S. aureus* is often associated with contaminated food.

❖ *Enterobacter:*

Enterobacter species cause infections, particularly in individuals with weakened immune systems.

❖ *Pseudomonas:*

Pseudomonas species are opportunistic pathogens that can cause infections, particularly in individuals with compromised immune systems.

❖ *Candida*

In the gut, an overgrowth of Candida, often referred to as candidiasis, can lead to gastrointestinal issues. This may include symptoms such as bloating, gas, constipation, or diarrhea.

5. Biosafety Profile of Bifidobacteria bifidum

Bifidobacterium bifidum, a naturally occurring bacterium in the human gastrointestinal tract, holds a **Generally Recognized as Safe (GRAS)** status. It is a probiotic microorganism commonly found in fermented foods and some dairy products. Its presence in the gut is considered beneficial for digestive health and immune system modulation (O'Callaghan & van Sinderen, 2016).

DRUG BANK has also approved and experimented *Bifidobacterium bifidum* for medicinal use under accession **ID DB16538**.

The non-invasive nature of *Bifidobacterium* is a key aspect of its biosafety profile. It coexists harmoniously with other commensal bacteria in the gut (Cohen et al., 2016; Esaiassen et al., 2017), promoting a balanced microbial environment. This bacterium lacks traits associated with pathogenicity and does not produce harmful toxins under normal conditions (Cohen et al., 2016; Esaiassen et al., 2017).

As a probiotic, *B. bifidum* contributes to the maintenance of a healthy gut microbiota. Its inclusion in various food products and supplements is based on its potential health benefits. However, it's important to note that while generally safe for the majority of the population, individuals with compromised immune systems or severe underlying health conditions should seek guidance before consuming probiotics, including *B. bifidum*. There have been reported instances of Bifidobacterium-mediated sepsis and bacteremia, underscoring the importance of cautious consideration, particularly in vulnerable populations (Kothari et al., 2019).

6. Significance of *Bifidobacteria bifidum* in CanXida Restore Formula

CanXida Restore Formula is strategically formulated to harness the diverse health properties of *Bifidobacterium bifidum*, offering a comprehensive solution for overall gut health. The probiotic's ability to attach to mucosal surfaces and colonize the gastrointestinal tract is pivotal, as it forms the foundation for restoring a harmonious equilibrium within the gut microbiota. This can promote a healthy and balanced microbial ecosystem, aligning with the formula's primary objective*****.

Moreover, CanXida Restore Formula can address a spectrum of gastrointestinal disorders by incorporating *Bifidobacterium bifidum*. This targeted approach underscores the formula's commitment to providing relief for a range of digestive concerns such as acid-related dyspepsia, diarrhea, abdominal pain, constipation, and gastric discomfort, inflammatory bowel diseases and irritable bowel syndrome*.

Furthermore, its lactic acid production ensures a balanced pH, creating an inhospitable space for harmful bacteria. The immune modulation and antimicrobial activity of *B. bifidum* enhance the formula's efficacy in targeting pathogens including Candida.

In conclusion, CanXida Restore Formula's strategic utilization of *Bifidobacterium bifidum's* diverse health properties not only aim to restore gut equilibrium but also addresses a wide spectrum of gastrointestinal concerns. With its commitment to promoting digestive health, managing inflammatory conditions, and targeting harmful pathogens, the formula stands as a comprehensive solution for overall gut health*.

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