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Original Article

Impact of Probiotic Lactic Acid Bacteria in the Management of Upper Respiratory Tract Infections

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Abstract

Upper respiratory tract infections (URTIs) are among the most prevalent infectious diseases globally, significantly impacting public health and healthcare systems. It concludes conditions such as the common cold, sinusitis, and pharyngitis, are prevalent and often lead to significant morbidity. Traditional management strategies primarily involve symptomatic treatment and in certain cases, antibiotics, which contribute to the growing problem of antimicrobial resistance. In recent years, probiotics specifically lactic acid bacteria (LAB) have emerged as promising adjuncts in the prevention and management of URTIs due to their immunomodulatory and antimicrobial properties. They offer a novel approach to managing URTIs. This research paper explores the impact of probiotic LAB on URTI incidence, severity, and duration across various populations. The study reviews both clinical trials and mechanistic studies to evaluate the effectiveness of specific LAB strains, such as Lactobacillus rhamnosus, Lactobacillus casei, and Lactobacillus plantarum, in modulating host immune responses and inhibiting pathogenic colonization in the upper respiratory tract. Evidence suggests that LAB enhance mucosal immunity by stimulating the production of secretory immunoglobulin A (sIgA), cytokines, and natural killer (NK) cell activity, thereby strengthening the host's first line of defense against respiratory pathogens. In addition, LAB may competitively inhibit pathogen adherence to mucosal surfaces and produce antimicrobial substances, such as bacteriocins and hydrogen peroxide, that directly suppress pathogenic microbes. Probiotic LAB, such as Lactobacillus rhamnosus GG and Lactobacillus casei, have demonstrated safety and tolerability, with adverse effects being rare and generally mild. Probiotic lactic acid bacteria represent a safe and effective complementary approach to managing URTIs by modulating host immunity and reducing pathogen load. Their integration into clinical practice could significantly contribute to non-antibiotic strategies for infection control, ultimately improving patient outcomes and mitigating antimicrobial resistance. Further large-scale, well-designed clinical trials are essential to establish standardized guidelines for probiotic use and their application in clinical practice of URTI management.

Keywords: *Probiotics, Lactic acid bacteria, Immunomodulation, URTI, Lactobacillus*

Introduction

An Upper Respiratory Tract Infection (URTI) refers to an infection affecting the upper portion of the respiratory system, including the nose, sinuses, throat, larynx (voice box), and trachea (windpipe). Common examples of URTIs are the common cold, sinusitis, pharyngitis, and laryngitis, are among the most prevalent infectious diseases worldwide. URTIs are primarily caused by viruses, with rhinoviruses being the most common culprits. Other viral agents include influenza viruses, parainfluenza viruses, respiratory syncytial virus (RSV), and coronaviruses. Bacterial infections, such as those caused by *Streptococcus pyogenes* leading to strep throat, can also result in URTIs. They account for a significant portion of healthcare visits and antibiotic prescriptions, leading to increased healthcare costs and concerns over antibiotic resistance. Traditional management strategies primarily focus on symptomatic relief, with limited options for prevention. This has prompted a search for alternative or complementary therapies that can effectively prevent or mitigate the impact of URTIs. Lactic acid bacteria (LAB) are a diverse group of Gram-positive, non-spore-forming bacteria known for their ability to produce lactic acid as a primary metabolic end product. They are commonly found in fermented foods and the gastrointestinal tracts of humans and animals.

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Certain strains of LAB, when consumed in adequate amounts, exert beneficial effects on the host and are thus classified as probiotics. Probiotics, particularly lactic acid bacteria (LAB), have garnered attention for their potential role in enhancing immune function and maintaining mucosal integrity, which are crucial in defending against respiratory pathogens. Strains such as *Lactobacillus rhamnosus* GG and *Lactobacillus casei* have been extensively studied for their beneficial effects on human health (Hojsak, I., et al 2010). Emerging evidence suggests that these probiotics may exert protective effects against URTIs through various mechanisms, including modulation of the immune system, competition with pathogens for adhesion sites, and enhancement of epithelial barrier function (Berggren, A., et al. 2011, De Boeck, I., et al 2021).). The rationale behind their use lies in their capacity to interact with the host's immune system and the resident microbiota in the gut, which has a well-established connection to the health of other mucosal sites, including the respiratory tract (the gut-lung axis) (Butler, C. C., et al. 2020). This paper aims to review the current literature on the role of probiotic LAB in the prevention and management of URTIs. We will examine the mechanisms by which LAB may influence respiratory health, evaluate the clinical evidence supporting their use, and discuss safety considerations. By synthesizing existing research, we aim to provide insights into the potential of probiotic LAB as a therapeutic strategy for URTIs.

Probiotic lactic acid bacteria that have been studied for their involvement in the management of Upper Respiratory Tract Infections (Kumpitsch, C., et al. 2019). Please note that the effectiveness can vary depending on the specific strain, dosage, and individual factors (Fujita, R., et al. 2013).

- *Lactobacillus rhamnosus* (various strains, including GG) (Hojsak, I., et al 2010).
- *Lactobacillus casei* (various strains, including Shirota) (Shida, K., et al 2017).
- *Lactobacillus paracasei* (various strains, including DN-114001 and HEAL 9) (Guillemard, E., et al 2010)
- *Lactobacillus acidophilus* (various strains, including NCFM)
- *Lactobacillus plantarum* (various strains, including DR7 and HEAL 9)
- *Lactobacillus delbrueckii* subsp. bulgaricus (strain OLL1073R-1) (Makino, S., et al 2010)
- *Streptococcus thermophilus* (various strains, including OLS3059)

It is often the case that probiotic products for URTIs contain a combination of different *Lactobacillus* and *Bifidobacterium* species to provide a broader range of potential benefits (Hao, Q., et al 2022). While *Bifidobacterium* are not strictly lactic acid bacteria, they are commonly included in probiotic formulations for URTIs and often work synergistically with *Lactobacillus*. Some commonly studied *Bifidobacterium* species include:

- *Bifidobacterium animalis* subsp. *lactis* (various strains, including Bb-12 and Bi-07)
- *Bifidobacterium breve* (strain 99)

Mechanisms of Action

Lactic acid bacteria (LAB) probiotics exert their beneficial effects in managing Upper Respiratory Tract Infections (URTIs) through several interconnected mechanisms.

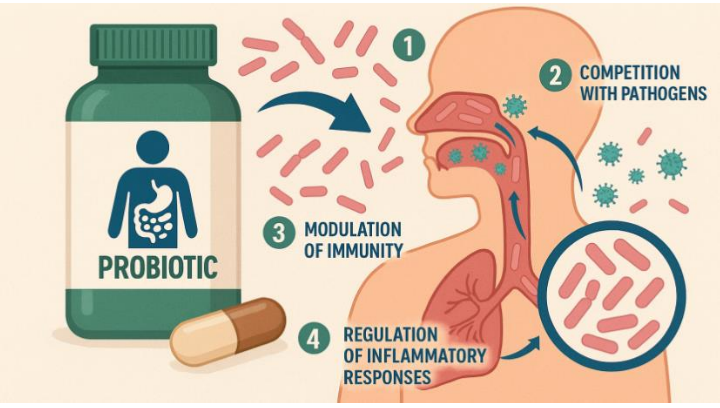

Figure 1: Showing different mechanism of probiotic lactic acid bacteria in the management of upper respiratory tract infections.

1. **Immunomodulation:** LAB can modulate the host's immune response by enhancing the activity of immune cells like macrophages and natural killer cells, increasing the production of specific immunoglobulins (IgA, IgG, IgM), and stimulating cytokine production (e.g., IL-10, IL-12, TNF-α). Which can then exert effects in the respiratory mucosa. Enhanced Phagocytic Activity: LAB can enhance the ability of immune cells like monocytes and polymorphonuclear leukocytes to engulf and destroy pathogens. Increased Cytokine Production: They can stimulate the production of various cytokines (e.g., IL-1, IL-2, IL-6, IL-10, IL-12, IFN-α, IFN-γ, TNF-α) that play crucial roles in coordinating the immune response against viral and bacterial infections. Some LAB strains can also induce the production of anti-inflammatory cytokines like IL-10, helping to regulate the immune response and prevent excessive inflammation in the respiratory tract (Merenstein, D., et al. 2010). Increased Secretory IgA (sIgA) Production: LAB can promote the production of sIgA in the gut mucosa. sIgA is then transported to mucosal surfaces, including the respiratory tract, where it can neutralize pathogens and prevent their adhesion to host cells (Vrese, M., et al 2006). Activation of Immune Cells: LAB can interact with intestinal epithelial cells and immune cells via Toll-like receptors, leading to the activation of T cells and natural killer (NK) cells, which are important for antiviral defense (Singh, R., et al. 2022). They can also stimulate T helper 1 (Th1) cells, known for their antiviral activity. Enhanced

Antigen Presentation: Certain LAB strains can enhance the antigen-presenting activity of dendritic cells, leading to improved activation of CD8+ T cells, which are crucial for eliminating virus-infected cells (Rashidi, K., et al 2021). Direct Interaction in the Respiratory Tract: Some evidence suggests that LAB or their components can translocate to the respiratory tract via mechanisms like microaspiration or esophageal reflux, where they might directly interact with the local immune system.

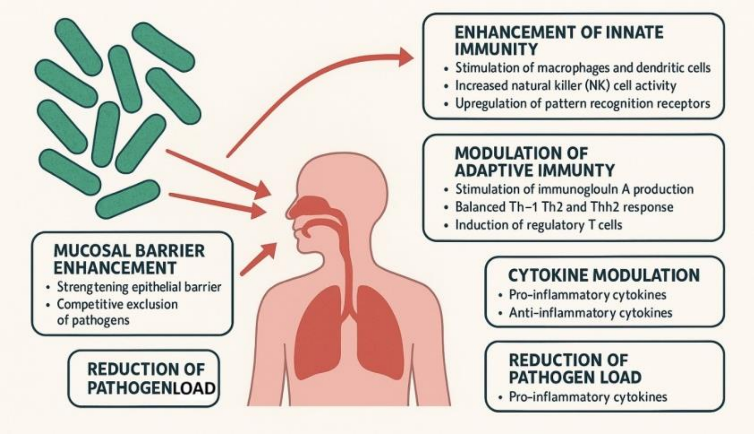

Figure 2: Showing mechanism of immunodulation by LAB strains in the management of upper respiratory tract infections.

2. **Pathogen Inhibition**: Certain LAB strains produce antimicrobial substances and compete with pathogens for adhesion sites, reducing colonization by harmful microbes like *Streptococcus pneumoniae* and *Haemophilus influenzae* (Gluck, U., et al 2003). Mechanisms of pathogen inhibition by LAB Strains includes Production of Organic Acids: LAB produce lactic acid and acetic acid, which lower pH and create an environment hostile to many pathogens. Acidification disrupts pathogen cell membranes and enzyme function (Rautava, S., et al 2009). Bacteriocin Production: LAB synthesize bacteriocins, which are proteinaceous toxins that inhibit closely related or even some distant microbial species. Examples are Nisin (produced by *Lactococcus lactis*), Pediocin (from *Pediococcus spp.*). Competitive Exclusion: LAB compete with pathogens for adhesion sites on intestinal epithelial cells and for nutrients (Huang, Y., et al. 2020). This prevents colonization by harmful microbes like *Salmonella*, *E. coli*, and *Listeria* in both the gut and potentially the upper respiratory tract. Immune System Modulation: LAB can enhance mucosal immunity by stimulating IgA production and cytokine release, improving host resistance to infection (Kumar, M., et al. 2014). s. Hydrogen Peroxide Production: Some LAB strains produce H_2O_2, which can inhibit anaerobic pathogens by oxidative stress.

Table 1: Mechanisms of Pathogen Inhibition by LAB Strains in URTI

LAB Strain	Inhibited Pathogens	Mechanism of Pathogen inhibition
Lactobacillus rhamnosus GG	*E. coli, Salmonella, Clostridium difficile*	Strong adhesion and immune modulation
Lactobacillus plantarum	*Listeria monocytogenes, Staphylococcus aureus*	Produces bacteriocins, good acid tolerance
Lactobacillus acidophilus	*Helicobacter pylori, Candida albicans*	Good mucosal colonizer
Lactococcus lactis	Gram-positive pathogens	Produces nisin
Pediococcus acidilactici	*Listeria, Salmonella*	Produces pediocin

3. **Epithelial Barrier Enhancement**: LAB can strengthen the mucosal barrier by upregulating tight junction proteins, thereby preventing pathogen translocation and maintaining mucosal integrity. LAB can enhance the integrity of the intestinal barrier by promoting tight junction protein expression and mucin production (Smith, T. J., et al 2021).. A healthy gut barrier can reduce the translocation of pathogens and inflammatory molecules, indirectly benefiting the respiratory system through the gut-lung axis. Mechanisms of Epithelial Barrier Enhancement by LAB includes Upregulation of Tight Junction Proteins: LAB promote expression of TJ proteins such as occludin, claudins, and zonula occludens-1 (ZO-1). This reinforces cell–cell adhesion and reduces intestinal permeability ("leaky gut"). *Lactobacillus rhamnosus* GG (LGG) increases ZO-1 and occludin expression. Mucin Production Stimulation: LAB induce mucin gene expression (e.g., MUC2), thickening the mucus layer and physically blocking pathogen contact. *Lactobacillus plantarum* stimulates mucin secretion in goblet cells. Modulation of Inflammatory Pathways: LAB reduce pro-inflammatory cytokines (e.g., TNF-α, IL-6) and promote anti-inflammatory cytokines (e.g., IL-10), preventing inflammation-induced TJ disruption. Some strains inhibit NF-κB activation, which otherwise weakens barrier function. Activation of Host Signaling Pathways: LAB can activate MAPK and PI3K/Akt pathways, which are involved in cytoskeletal integrity and TJ assembly. *Lactobacillus reuteri* is known to modulate epithelial signaling cascades that regulate barrier homeostasis. Production of Metabolites (SCFAs): Some LAB strains ferment carbohydrates to produce short-chain fatty acids (e.g., butyrate, acetate), which fuel epithelial cells and support TJ integrity.

Table 2: mechanisms of Epithelial Barrier Enhancement by LAB Strains in URTI (Uehara, Y., et al 2000)

LAB Strain	Barrier-Enhancing Actions	Mechanisms of Epithelial Barrier Enhancement
Lactobacillus rhamnosus GG	Upregulates ZO-1, occludin; reduces inflammation	Tight junction reinforcement, cytokine modulation
Lactobacillus plantarum	Enhances mucin expression and TJ proteins	Mucin layer thickening, TJ gene expression
Lactobacillus reuteri	Modulates TLR and PI3K/Akt signaling; anti-inflammatory	Host signaling pathway activation
Bifidobacterium bifidum (technically not LAB but synergistic)	Strengthens TJ and immune response	Cytokine balance, TJ protein expression

4. **Modulation of Gut Microbiota:** Certain LAB strains can inhibit the adhesion and growth of pathogenic microorganisms in the respiratory tract. For instance, *Lactobacillus Lacti, ,Lactobacillus casei, Lactobacillus rhamnosus GG* has been shown to interfere with the adherence of *Moraxella catarrhalis* to human airway epithelial cells by approximately 50%. Additionally, *Lactobacillus acidophilus* strains possess auto-aggregation properties and can co-aggregate with pathogens, thereby preventing their colonization (Santamaria, F., et al. 2020). Restoration of Microbial Balance: LAB can help restore a balanced gut microbiota, which is crucial for overall immune health (Weizman, Z., et al 2005). A diverse and healthy gut microbiome can contribute to a more effective immune response against respiratory pathogens. The specific mechanisms and efficacy can vary significantly depending on the strain of lactic acid bacteria, the dosage, and the individual's health status. Competitive Exclusion of Pathogens: LAB compete for nutrients and adhesion sites on the intestinal epithelium, preventing colonization by harmful bacteria (e.g., *E. coli, Salmonella*). This mechanism helps shift the microbial balance toward beneficial species (Zhao, Y., et al 2022). LAB produce organic acids (lactic, acetic), hydrogen peroxide, and bacteriocins, which lowers intestinal pH, inhibit growth of pathogens and favour acid-tolerant beneficial microbes (e.g., *Bifidobacterium*). LAB stimulate beneficial microbes and create an environment conducive to the growth of commensal bacteria like *Bifidobacterium spp.* and *Faecalibacterium prausnitzii*. The reason behind these actions are Cross-feeding (e.g., providing metabolic byproducts like lactate), decreasing oxidative stress and Short-Chain Fatty Acid (SCFA) production. LAB contribute to SCFA production (directly or indirectly), especially acetate and lactate, which inhibit pathogenic microbes, support colonocyte health and influence gut microbial composition by favoring anaerobes.nSome LAB strains interfere with quorum sensing signals used by pathogens to regulate virulence and biofilm formation, indirectly benefiting commensal microbes. Certain LAB produce lactonases or acylases that degrade N-acyl homoserine lactones (AHLs), common QS signals in Gram-negative bacteria. LAB may release mimic molecules or antagonists that block receptors used in QS systems of pathogens like Pseudomonas aeruginosa or *Staphylococcus aureus*. By interfering with QS, LAB can reduce biofilm formation, making pathogens more susceptible to immune clearance and antibiotics. Inhibiting QS and pathogenic biofilms reduces competition and allows beneficial microbes to colonize more effectively.

Table 3: Mechanisms of Gut Microbiota Modulation by LAB in URTI (Li, L., et al 2020; Lazou Ahrén, I., et al 2021)

LAB Strain	Microbiota Modulatory Effects	Mechanisms of Gut Microbiota Modulation by LAB
Lactobacillus rhamnosus GG	Increases *Bifidobacteria*, reduces *Clostridium spp.*	Competitive exclusion, immune modulation
Lactobacillus plantarum	Enhances microbial diversity	Bacteriocin and SCFA production
Lactobacillus casei	Promotes *Lactobacillus* and *Bifidobacterium* growth	Acetate production, pH lowering

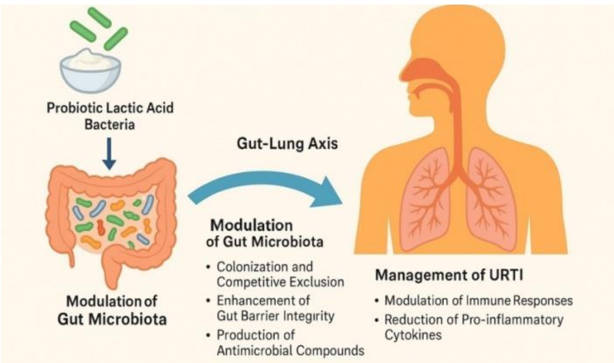

Figure 3: Showing modulation of gut microbiota by probiotic LAB in the management of URTI

Clinical Evidence

Adults: A systematic review and meta-analysis of randomized controlled trials indicated that probiotic supplementation reduced the incidence and duration of URTIs in adults. The studies reported a significant decrease in URTI episodes and a reduction in the average duration of infections (Damholt, M. B., et al. 2022).

Children: In pediatric populations, LAB supplementation has been associated with a decreased incidence of URTIs and reduced antibiotic usage. For instance, *Lactobacillus rhamnosus* GG has demonstrated efficacy in reducing respiratory infections and acute otitis media in children (Hatakka, K., et al 2001).

Elderly: Older adults may benefit from LAB supplementation through enhanced immune responses and reduced URTI incidence. Studies have shown that specific LAB strains can improve mucosal immunity and decrease the frequency of respiratory infections in this demographic (Wang, Y., et al 2021).

Table 4: Effect of LAB strains in different target group of URTI (Leyer, G. J., et al 2009; Langkamp-Henken, B., et al. 2015; Li, L., et al 2020; Lazou Ahrén, I., et al 2021)

Strain	Key Benefit	Target Group	Delivery Form
L. rhamnosus GG	Fewer colds, faster recovery	Children, athletes	Capsules, dairy
L. casei Shirota	Fewer sick days	Adults	Fermented drinks
L. plantarum HEAL9	Reduced symptom severity	General population	Capsules
S. salivarius K12	Prevents strep/tonsillitis	Children	Lozenges
L. reuteri DSM 17938	Decreased URTI frequency	Children	Drops
L. paracasei 8700:2	Immune enhancement	Adults	Tablets, capsules

Safety and Tolerability

Probiotic LAB are generally considered safe for consumption. Adverse effects are rare and typically mild, including gastrointestinal symptoms such as bloating and gas. However, caution is advised for immunocompromised individuals, and consultation with healthcare providers is recommended before initiating supplementation.

Limitations and Future Directions

While evidence supports the beneficial role of LAB probiotics in URTI management, several limitations exist. Strain Specificity: Not all LAB strains confer the same benefits. Further research is needed to identify the most effective strains. Dosage and Duration: Optimal dosing regimens and treatment durations remain to be established. Population Diversity: Most studies have been conducted in specific populations, limiting generalizability. Future research should focus on large-scale, multicenter RCTs to address these gaps and provide more definitive recommendations.

Conclusion

Probiotic LAB, notably strains like *Lactobacillus rhamnosus* GG and *Lactobacillus casei*, show promise in the prevention and management of URTIs across various age groups. Their multifaceted mechanisms immunomodulation, pathogen inhibition, and epithelial barrier enhancement contribute to their efficacy. While current evidence supports their use, further large-scale, high-quality studies are necessary to establish standardized guidelines for their application in respiratory health. Probiotic lactic acid bacteria (LAB) have emerged as a promising adjunct in the prevention and management of upper respiratory tract infections (URTIs). Clinical studies and meta-analyses indicate that LAB supplementation can reduce the incidence, duration, and severity of URTIs across various populations, including children, adults, and the elderly. These benefits are attributed to LAB's ability to modulate the immune system, enhance mucosal barrier function, and inhibit pathogenic microorganisms. The safety profile of LAB probiotics is generally favorable, with most adverse effects being mild gastrointestinal symptoms. However, caution is advised for immunocompromised individuals, and further research is needed to establish optimal strains, dosages, and treatment durations. while LAB probiotics are not a standalone treatment, their integration into daily health regimens offers a viable strategy to bolster respiratory health and reduce reliance on antibiotics. Ongoing research and well-designed clinical trials will be essential to fully elucidate their role and maximize their therapeutic potential in URTI management.

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Conflicts of interest

There are no conflicts of interest.

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