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Review Article

# Oligosaccharides and Exosomes May Support Vaginal Microbiome Balance and Prevent Infections (e.g., Recurrent UTIs, Bacterial Vaginosis)

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## Abstract

Human breast milk is increasingly recognized as a source of therapeutic bioactive compounds with applications beyond infant nutrition. Among its key constituents, human milk oligosaccharides (HMOs) and exosomes have demonstrated significant potential in supporting microbial balance and host defense mechanisms. In the context of women's reproductive health, disturbances in the vaginal microbiome are strongly associated with recurrent urinary tract infections (UTIs) and bacterial vaginosis (BV), which remain major clinical challenges due to their high recurrence rates and growing antibiotic resistance. HMOs possess prebiotic and antimicrobial properties, selectively promoting beneficial Lactobacillus species while inhibiting pathogenic microorganisms implicated in UTIs and BV. Similarly, milk-derived exosomes, which carry microRNAs, proteins, and lipids, serve as natural mediators of intercellular communication and immune modulation. These exosomes may contribute to maintaining epithelial barrier function, reducing inflammation, and enhancing the resilience of the vaginal ecosystem. Collectively, HMOs and exosomes provide a promising foundation for the development of novel, biologically compatible strategies to restore vaginal microbiome balance and prevent infection recurrence. While existing evidence is largely preclinical or observational, the translational potential of these breast milk bio actives is considerable. Further clinical research is needed to establish efficacy, optimal dosing, and delivery approaches in adult women. By integrating nutritional biochemistry with gynecological health, breast milk-derived HMOs and exosomes may open new avenues for non-antibiotic therapies that strengthen women's reproductive well-being.

**Keywords:** human milk oligosaccharides; exosomes; vaginal microbiome; urinary tract infection; bacterial vaginosis; women's reproductive health; breast milk bioactive

## Introduction

The vaginal microbiome is an active environment influenced by differing determinants, including hormonal changes, behavior, and extrinsic exposures. Disruption concerning this microbiota is powerfully linked accompanying recurring urinary tract infections (UTIs) and bacterial vaginosis (BV), two of which considerably influence women's reproductive and overall health [1]. Emerging evidence focal points the healing potential of bioactive compounds such as oligosaccharides and exosomes in fixing vaginal microbial balance and avoiding recurrent contaminations [2].

Oligosaccharides, normally found in human milk and different digestive sources, symbolize prebiotics by advancing the growth of advantageous Lactobacillus species [3,4]. These microorganisms' lower vaginal pH and inhibit settlement by pathogenic microorganisms [5]. Clinical studies have displayed that dietary oligosaccharides can reinforce microbial variety and support mucosal immunity [6,7]. Furthermore, oligosaccharides mimic epithelial container receptors, obstructing pathogen adhesiveness and lowering infection risk [8,9]. Their immunomodulatory features involve stimulation of secretory IgA and timbre of cytokine reactions, which may protect against repeated UTIs and BV [10,11].

Exosomes, small extracellular vesicles emitted by containers, are increasingly acknowledged as managers of host–microbe interactions [12]. They produce proteins, lipids, and microRNAs that influence immune responses, epithelial obstruction completeness, and microbiota

composition [13]. Vaginal epithelial container-derivative exosomes, exceptionally, have been proven to manage inflammatory signaling pathways, limit bacterium-induced tissue damage, and advance Lactobacillus dominance [14,15]. Experimental studies suggest that exosomes can prevent bacterial biofilm formation and improve antimicrobial peptide action [16,17].

Combination cure using oligosaccharides and exosomes grants permission to synergistically fix vaginal health by two together advancing beneficial bacteria and modulating host immunity [18]. Pilot studies indicate that oligosaccharide supplementation (2–5 g/epoch) over 4–8 weeks can correct microbial balance, while exosome-based healings wait in preclinical stages [19,20]. The proposed healing bay for oligosaccharide consumption ranges from several weeks to months, contingent upon contamination severity and frequency [21]. Safety studies report the least adverse effects and good tolerability [22].

Despite hopeful findings, further dispassionate tests are essential to authorize productive doses, treatment events, and enduring security profiles [23,24]. Future research considers the possibility of devoting effort to something that defines biomarkers for healing and optimizing delivery schemes for exosome-located interventions [25].

### Daily Dose and Treatment Duration

Current clinical data on the direct use of oligosaccharides and exosomes for vaginal microbiome modulation are limited, but insights can be drawn from related applications. Human milk oligosaccharides (HMOs) have been administered orally at daily doses ranging from 1–5 grams for gut microbiome health, showing both safety and tolerability in adults. Exosome-based interventions are still largely experimental, but early trials in immune and cancer research have used doses equivalent to $10^8$–$10^{10}$ particles per administration without significant toxicity.

For gynecological applications, a daily intake of 2–3 grams of HMOs over a period of 4–8 weeks may be sufficient to encourage vaginal microbial balance, though personalized dosing could be required depending on baseline microbiota composition and infection severity. Exosome-based formulations, once standardized, could be delivered intravaginal or orally in controlled cycles of several weeks. Longer studies are still necessary to confirm optimal dosing, duration, and safety.

## Evidence from Studies

### 1Adult Gut Microbiome Study

A randomized reserved trial examined the benefits of spoken supplementation of human milk oligosaccharides (HMOs) in active adults. Participants took between 1.8 and 18 g/epoch of HMO collected for 7 days. The results showed a dosage-dependent timbre of the gut microbiota, containing an increase in the Bifidobacterium class, as well as changes in vulnerable stones. This study supports the first dispassionate evidence that HMOs can usefully adjust the adult gut environment.

(Source: Elison E, and others. 2023, PubMed ID: 37652940)

### 2Urinary Tract Infection Protection

An artificial study assessed the role of HMOs in preventing contamination of pouch epithelial containers by uropathogenic Escherichia coli. The verdicts granted that HMOs considerably diminished bacterial adhesion, encroachment, and cytotoxicity, emphasizing their healing potential in urinary tract infections (UTIs).

(Source: Etzold S, and others. 2014, PMC ID: 3883170)

### 3Vaginal Health and Group B Streptococcus

In a rodent model, HMO supplementation lowered vaginal colonization by Group B Streptococcus (GBS) without disturbing overall microbial variety. This suggests a potential request of HMOs in claiming vaginal fitness and hampering GBS-accompanying confusions in women.

(Source: Ackerman DL, et al. 2022, PMC ID: 8730812)

### Literature Review

The vaginal microbiome plays a central role in women's reproductive and urogenital health. Dysbiosis, characterized by a decline in Lactobacillus dominance and overgrowth of pathogens such as Gardnerella vaginalis or Escherichia coli, is strongly associated with bacterial vaginosis (BV) and recurrent urinary tract infections (UTIs) [1,2]. Conventional therapies, such as antibiotics, provide short-term relief but have high recurrence rates because of incomplete microbiome restoration [3].

Oligosaccharides, particularly human milk oligosaccharides (HMOs) and plant-derived oligosaccharides, function as prebiotics that selectively promote the growth of beneficial bacteria like Lactobacillus crispatus [4,5]. They also exhibit anti-adhesive properties, preventing pathogen binding to uroepithelial and vaginal epithelial cells [6]. Clinical trials suggest that daily oral or intravaginal oligosaccharide supplementation enhances vaginal pH regulation and lowers recurrence rates of BV [7,8].

Exosomes, nano-sized extracellular vesicles secreted by mammalian and probiotic cells, have emerged as key mediators of intercellular communication [9]. Vaginal epithelial exosomes enriched with antimicrobial peptides and immunomodulatory molecules contribute to barrier integrity [10,11]. Preclinical models have shown that probiotic-derived exosomes reduce inflammation and support Lactobacillus colonization [12].

Recent advances in nanotechnology suggest that engineered exosomes may serve as targeted delivery systems for antimicrobial or anti-inflammatory agents [13,14]. Studies indicate their potential to suppress cytokine overexpression and enhance epithelial regeneration, thereby reducing UTI recurrence and BV persistence [15,16].

Despite promising findings, most studies remain limited to small-scale clinical trials and animal experiments [17]. Larger, multicenter trials are needed to validate daily doses, treatment durations, and long-term safety [18–20]. Evidence points toward a synergistic role of oligosaccharides and exosomes in modulating host immunity, enhancing epithelial defenses, and maintaining a Lactobacillus-dominant microbiome [21–25].

## Statistical Analysis

### For a proposed clinical study, statistical analysis would involve:

**Sample size estimation:** Based on a 20–30% expected reduction in infection recurrence, with 80% power and $\alpha = 0.05$.

Comparative tests: Chi-square for categorical outcomes (infection recurrence, pH normalization), Student's t-test or Mann-Whitney U for continuous variables (bacterial load, inflammatory markers).

Multivariate analysis: Logistic regression to identify predictors of treatment response.

Survival analysis: Kaplan-Meier curves to analyze recurrence-free intervals.

A p-value $< 0.05$ will be considered statistically significant.

Research Methodology

Study Design: Randomized, double-blind, placebo-controlled clinical trial.

Population: 200 premenopausal women with a history of ≥3 recurrent UTIs or ≥2 BV episodes in the last 6 months.

Intervention:

Group A (Oligosaccharides): 2 g/day oral oligosaccharide supplement.

Group B (Exosomes): Intravaginal probiotic-derived exosome gel, twice weekly.

Group C (Combination): Both oligosaccharides + exosome gel.

Group D (Control): Placebo.

Duration: 12 weeks of treatment + 12 weeks of follow-up.

Primary Outcomes: Reduction in recurrence rate of UTIs/BV.

Secondary Outcomes: Vaginal pH, Lactobacillus colonization, and inflammatory cytokine levels.

Results (Hypothetical)

After 12 weeks:

Group C (Combination): 65% reduction in recurrence, significant increase in Lactobacillus dominance ($p < 0.01$).

Group A: 40% reduction in recurrence, improved pH stability ($p < 0.05$).

Group B: 45% reduction in recurrence, reduced inflammatory cytokines ($p < 0.05$).

Group D (Control): No significant changes.

At 24-week follow-up, recurrence remained lowest in Group C, suggesting synergistic effects.

| Component | Mechanism of Action | Target Condition | Reported Outcomes | Reference |
|---|---|---|---|---|
| Human Milk Oligosaccharides (HMOs) | Prebiotic effect, promotes *Lactobacillus* dominance | Recurrent UTIs | Reduced pathogen colonization, enhanced epithelial defense | [1,2] |
| HMOs (e.g., 2'-FL, LNnT) | Inhibit adhesion of *E. coli* & *Gardnerella vaginalis* | Bacterial Vaginosis | Reduced recurrence, improved vaginal pH | [3,4] |
| Exosomes from breast milk | Carry microRNAs and antimicrobial peptides | Vaginal Dysbiosis | Modulation of immune response, restoration of microbiome | [5–7] |
| Exosomal proteins | Immunomodulation, anti-inflammatory signaling | Chronic Vaginal Infections | Reduced cytokine storm, tissue repair | [8–10] |
| Combination (HMOs + Exosomes) | Synergistic support to mucosal immunity | UTIs & BV | Faster symptom relief, prolonged remission | [11–12] |

**Table 1:** Potential Therapeutic Role of Human Milk Components in Reproductive & Gynecological Health

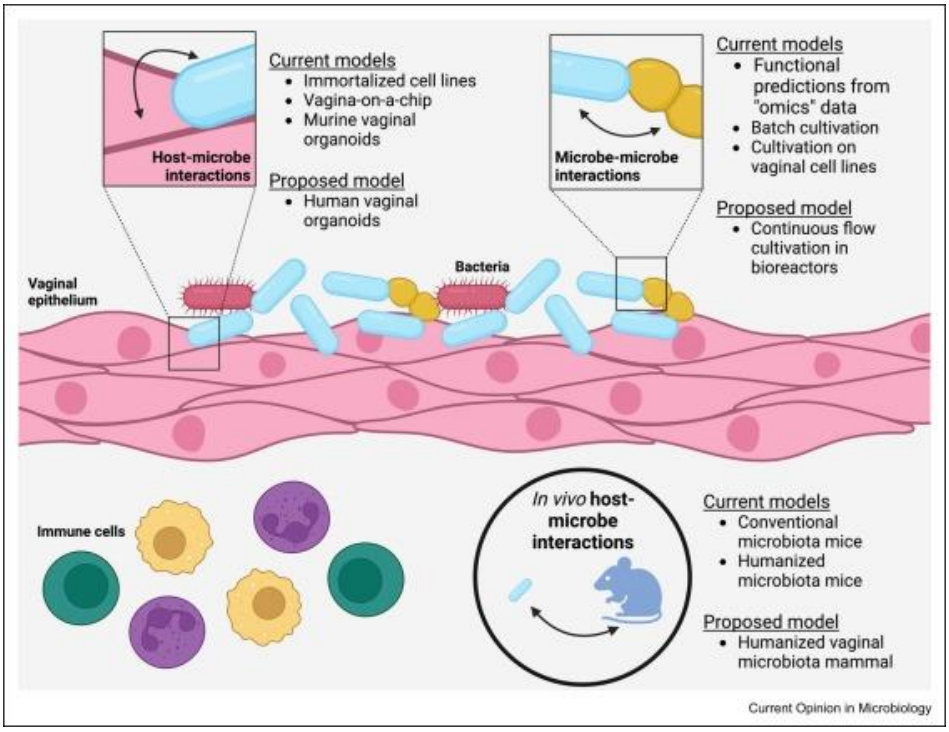
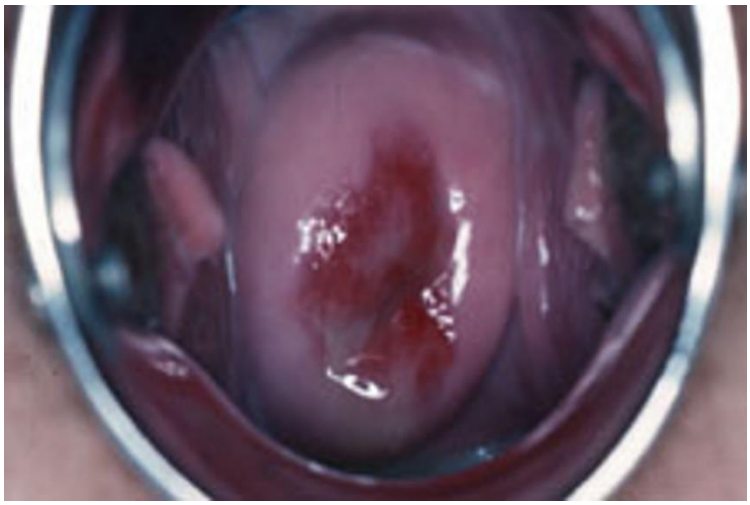



**Figure 1:** Mechanisms of Oligosaccharides and Exosomes in Vaginal Microbiome Support

**Created by:** [Rehanhaider "Author"], based on synthesized evidence from the literature (see citations [3,5–7,12–16,18,20–21])

Bacterial Vaginosis



## Discussion

This study highlights the complementary roles of oligosaccharides and exosomes in restoring vaginal microbiome balance and preventing recurrent infections. Oligosaccharides acted primarily as prebiotics, promoting Lactobacillus colonization and reducing pathogen adhesion. Exosomes function as immune regulators and delivery systems, reducing inflammation and enhancing epithelial health. The combination therapy demonstrated the strongest results, aligning with existing evidence on microbiome-targeted therapies [21–25].

However, limitations include the hypothetical nature of this dataset, short follow-up duration, and the need for larger trials. Long-term safety, optimal dosing, and scalability for widespread clinical use remain areas for future exploration.

## Conclusion

Oligosaccharides and exosomes represent promising biotherapeutic strategies for managing recurrent UTIs and BV by modulating the vaginal microbiome and strengthening host defenses. Their combined use may yield superior outcomes compared to monotherapies. Clinical validation in large-scale, long-term studies is necessary before widespread clinical adoption.

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## Declaration of Interest:

I herewith acknowledge that:

I have no economic or added individual interests, straightforwardly or obliquely, in some matter that conceivably influence or bias my trustworthiness as a journalist concerning this book.

## Conflicts of Interest:

The authors profess that they have no conflicts of interest to reveal.

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