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Evaluating the Impact of *Weissella* as A Probiotic Intervention on Vaginal Health Outcomes: A Systematic Review of In vitro and Pre-clinical Evidence

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Abstract

Probiotics are gaining recognition for their role in preserving vaginal health. The human vagina is primarily inhabited by lactic acid bacteria (LAB), particularly *Lactobacillus*, which assist in regulating vaginal pH and preventing pathogen colonization. *Lactobacillus* has been extensively researched as a probiotic, particularly for its role in enhancing vaginal health by restoring a balanced microbiota. Probiotics may assist in alleviating therapy-related side effects during the treatment of vaginal infections or cervical cancer. Particularly, probiotic *Weissella,* which is a Gram-positive, catalase-negative coccoid or rod-shaped LAB, is currently being explored for management of vaginal health. The present systematic review synthesized current evidence on the role of *Weissella* species in promoting vaginal health. Among 1,248 records identified through database searching, seven studies met the predefined inclusion criteria. These investigations explored the antimicrobial, immunomodulatory, and antineoplastic properties of various *Weissella* strains, suggesting their potential application in strategies aimed at improving vaginal health outcomes. This review suggests that *Weissella* spp. can help to promote vaginal health by maintaining vaginal pH, preventing growth of pathogens; activating natural killer (NK) cell activity and exhibiting anticancer activity against cervical cancer. While evidence from in vitro and pre-clinical studies are significant, further clinical trials need to be undertaken in this area for its therapeutic potential. Evidence concerning the role of *Weissella* spp. in vaginal health remains scarce. A synthesis of the accessible literature is required to appraise the current state of knowledge, identify unresolved research questions, and inform future investigations into the probiotic potential of *Weissella* species.

Keywords: Vaginal Infection, Vaginal Health, Immunomodulation, Probiotics, *Weissella*, Systematic Review

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INTRODUCTION

Probiotics are increasingly getting recognized in the context of maintaining vaginal health. Human vagina is predominated by the lactic acid bacteria (LAB) such as *Lactobacillus* that help in maintaining vaginal pH and inhibit colonization of pathogens. *Lactobacillus* has been studied extensively as probiotics and their role in promoting vaginal health by restoring healthy microbiome.[1,2] Probiotics can also help in mitigating therapy-associated side effects during the treatment of vaginal infection or cervical cancer.[3,4] Recently, genus *Weissella*, a relatively less explored group of LAB, has been considered for their potential anti-bacterial, anti-oxidant, anti-inflammatory and anti-cancer activity.[5-7] *Weissella* are Gram-positive, catalase-negative, coccoid or rod-shaped LAB. So far, only few species of *Weissella* have been identified, including *Weissella sagaensis*,[8] *Weissella paramesenteroides*[9] that isolated from fermented dairy products; *Weissella beninensis,*[10] *Weissella fabalis,*[11] *Weissella viridescens,*[12] *Weissella uvarum,*[13] *Weissella cibaria, Weissella confuse*,[14] *Weissella koreensis,*[15] *Weissella thailandensis*[16] from fermented plant-based foods; *Weissella bombi,*[17] *Weissella cryptocerci,*[18] *Weissella muntiaci,*[19] *Weissella ceti*[20] from insects or animals, and *Weissella confusa, Weissella cibaria* isolated from human specimen.[21] Among the *Weissella* species, not all are regarded as GRAS (Generally Recognized as Safe), but a few species have cleared all parameters to become a potential candidate for probiotics. For instance, probiotic *W. confusa,*[22] *Weissella kimchi,*[23] *W. thailandensis,*[24] *W. cibaria,*[25] *W. paramesenteroides*[26] have been reported to have antimicrobial, anti-inflammatory and anticancer properties showing their various therapeutic applications.

Their function in maintaining vaginal flora is still poorly studied. Analyzing available scientific literature will assist in understanding their physiological role, identifying scarcity in knowledge, and providing support for future investigation exploring possible application of these bacteria as probiotic agents in vaginal flora.

Hence, the present systematic review aims to critically evaluate and consolidate existing literature on the health advantages of *Weissella* with specific focus on the vaginal health. By identifying current trends, strengths, and gaps in the literature, this review seeks to provide a foundation for future research and potential clinical applications of *Weissella*-based probiotic therapy in the vaginal health.

MATERIALS AND METHODS

Study design and registration

The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The study registered with International Prospective Register of Systematic Reviews (PROSPERO) (Registration No: CRD42025644349) before commencing the review process. This registration included detailed specifications regarding research questions, inclusion criteria, and planned analytical approaches.

The review process incorporated several key stages: (1) development of a standardized protocol with clearly defined objectives and methodology; (2) execution of a comprehensive, multi-database literature search; (3) implementation of rigorous study selection procedures with predefined eligibility criteria; (4) systematic data extraction and quality assessment; and (5) appropriate statistical synthesis of results where feasible.

Information sources and search strategy

The search strategy covered multiple databases from inception until March 2025: PubMed/MEDLINE, Scopus, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection and CINAHL (for patient-reported outcomes). Further, to minimize publication bias, following some additional Grey Literature and Trial Registries sources were included: ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP), OpenGrey, ProQuest Dissertations and Theses Global. The search strategy was designed in consultation with a medical librarian and combined Medical Subject Headings (MeSH) and free-text terms. No language restrictions were applied, with non-English articles translated for full-text review when necessary. The search strategy for PubMed and other databases is provided in the Supplementary material. We

also did complementary search approaches that involved manual review of reference lists from all incorporated studies and relevant review articles, forward citation searching via Google Scholar for papers citing key articles and correspondence with corresponding authors of included studies to identify unpublished data or ongoing research.

Eligibility criteria

Explicit eligibility criteria were established using the Population, Intervention, Comparator, Outcomes, Study Design (PICOS) framework to dire study selection:

Population

Inclusion criteria comprised studies with Experimental models

In vitro studies utilizing cell lines or in vivo models that could provide mechanistic insights into effect of *Weissella* on vaginal health.

Interventions

Any probiotic formulation containing *Weissella* species (e.g., *W. cibaria*, *W. confusa*, *W. viridescens*), all administration routes (oral, intravaginal), any treatment duration, various delivery vehicles (capsules, suppositories, fermented foods).

Comparators

Placebo controls (e.g., maltodextrin, saline), no treatment arms, active comparators (other probiotics, antibiotics, or antifungals).

Outcomes

Primary outcome measures focused on microbiological, immunological and pre-clinical outcomes.

Types of studies

Pre-clinical studies with comparator groups, controlled in vitro studies using cell lines.

Exclusion criteria

Studies involving pregnant or postmenopausal women due to the confounding effects of hormonal fluctuations on vaginal microbiota.

Reports lacking control groups or clear diagnostic criteria.

Case reports, case series, narrative reviews, conference abstracts without full data, or duplicate publications.

Selection process

After removing duplicates through Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), Title and abstract screening were done by two independent reviewers for eligibility criteria using the predefined PICOS framework. The full texts of all relevant studies were independently evaluated by two reviewers. Any discrepancies were addressed through discussion, when required, a third reviewer was also referred. Selection procedure for the study was summarized using a PRISMA 2020 flow diagram.

Data collection and extraction

Independent data extraction was done by two reviewers using the standardized data extraction parameters (Supplementary material). Discrepancies were resolved through consensus discussion. Where there was inadequate documentation, the study authors were contacted for additional information. In order to ensure consistency, the extracted data was independently verified by a third reviewer. The following standards were developed:

Risk of bias and quality assessment

Study quality was evaluated using design-appropriate tools. Cochrane Risk of Bias 2 (RoB 2) tool was used to assess randomized controlled trials. The tool assessed bias against five domain as mentioned in the literature.[27] Each domain received judgment as “low risk”, “some concerns”, or “high risk” of bias. The Quality Assessment Tool for in vitro studies (QUIN) assessed for study design and objectives, cell line characterization, experimental conditions, outcome measures and data analysis and reporting.

Each outcome evidence certainty was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. The evidence was classified into four groups depending on the level of certainty, which was either high, moderate, low, or very low certainty, depending on the amount of confidence in the study findings. The assessment considered

Table 1. Data extraction of included studies

Study (Year)	Experimental Design	Population/Cell Line	*Weissella* Strain	Intervention Details	Comparator	Key Outcomes
Lee[22]	In vitro	*C. albicans* CCARM14020, *E. coli* (CCARM 1360), *S. aureus* (CCARM 3703), vancomycin-resistant *Enterococcus* faecium (VRE; CCARM 5100) and T24 human bladder epithelial cells	*W. confusa* PL9001	*W. confusa* PL9001 (1×10^8 CFU), each pathogen (1×10^7 CFU), 30 min interference assay	No probiotic	Least ↓ *E. coli* by 3.17% and the highest ↓ *S. aureus* by 42.43% in interference assay.
Lee[23]	In vitro	*Candida albicans, E. coli, S. aureus*, *S. agalactiae* and Vaginal epithelial cells	*W. kimchii* PL9023	Interference test: *W. kimchi* (10^8 CFU/mL), vaginal cells (2×10^4 cells/ml), each pathogen ($1\text{-}2\times10^6$ cells/ml), 30 min adherence time	No probiotic	*W. kimchi* ↓ the adherence of *S. aureus* at pH 4.4 ($P < 0.001$) to vaginal cells in interference test
Thamacharo-ensuk et al.[24]	In vitro	Murine macrophage cell lines J774A.1	*Weissella* spp. (Thai isolate)	*Weissella* spp. (10^8 CFU/mL), J774A.1 cells (2.5×10^5 cells per well). 24 hrs incubation	*Lactobacillus acidipiscis* SR7-1 and *Lactobacillus farraginis* SL4-1, *Lactobacillus plantarum* NRIC 1067^T	*W. cibraria* PC86-2 ↑ IL-12, ($P < 0.01$) higher than the other *Weissella* spp.
Oh and Lee[25]	Pre-clinical	Mice NK cells	*W. cibaria* JW15	Once daily for 14 days via oral gavage	*Lactobacillus rhamnosus* GG ATCC 53103	↑NK cell activity ($P < 0.001$) and enhance cytotoxicity ($P < 0.001$) against tumor cells on increased ratio of JW15 to splenocyte
Amer et al.[26]	In vitro	Five different pathogens, *Bacillus subtilis, S. aureus, E. coli, P. aeruginosa, C. albicans* (10^5 cells/ ml)	*W. paramesen-teroides* MN2C2 filtrate against pathogens, Exopolysaccharides nanoparticles (EPS-NPs) isolated from *W. paramesen-teroides* MN2C2	100 µl of filtrate, 1.3 mg/ml for crude nano-EPS, 48 hrs	No comparator	Inhibition zone of 25 and 19 mm against *B. subtilis* and *P. aeruginosa,* respectively.

Table 1. Cont...

Study (Year)	Experimental Population/Cell Line Design		*Weissella* Strain	Intervention Details	Comparator	Key Outcomes
Choi and Yun[28]	Pre-clinical	CT26 and MC38 cell transplanted mice	*W. cibaria* WIKIM28	0.1 ml ($1x10^9$ CFU) injected intravenously to the tail of transplanted mice for 12-16 days.	With control (phosphate-buffered saline)	Colorectal tumor cells reduction was observed in terms of tumor volume (mm^3), against CT26 (P = 0.04969) and MC38 (P = 0.000091) in just 16 and 12 days, respectively.
Lee et al.[29]	In vitro	Antifungal activity against *C. albicans*	*W. confusa* WIKIM51 (Wilac D001)	1×10^7 CFU of *W. confusa* suspension for *C. albicans* inhibition for 24 hrs.	Sertaconazole nitrate and *Lactobacillus* spp.	Inhibited *C. albicans* growth (P < 0.001)

several areas such as risk of bias, consistency of the findings between studies, directness of evidence, precision, and publication bias.

Data synthesis and statistical analysis

During the analysis, if three or more studies reported comparable outcomes with sufficient methodological homogeneity, quantitative synthesis or meta-analysis was conducted. We used Mean difference (MD) or standardized mean difference (SMD) with 95% CIs for continuous outcomes. For dichotomous outcomes, we used Risk ratios (RR) with 95% confidence intervals (CIs). We used Random-effects models (DerSimonian-Laird method) for expected clinical and methodological heterogeneity in the data. I^2 statistic and Cochran's Q test were used for assessing heterogeneity. Evaluation with $P < 0.10$ was considered to be statistically significant. We performed sensitivity analyses by testing the Robustness of findings through the exclusion of studies with a high risk of bias**,** comparison of alternative statistical models (fixed-effect vs. random-effects) and influence analysis by sequentially removing each study. In qualitative synthesis, outcomes unsuitable for meta-analysis due to clinical or methodological heterogeneity, thematic analysis is applied for grouping of studies by common themes (e.g. antimicrobial effects, immunomodulation), identification of patterns across studies and highlighting of consistent and contradictory findings**.**

RESULTS

Study selection

A total of 1,248 studies were initially examined after database searches. Full text of fifty-one articles was evaluated for eligibility after duplicate removal and screening. Out of these, seven studies convinced the inclusion criteria and were incorporated in the qualitative synthesis. The study selection process is represented in the PRISMA flow diagram (Figure).

Study characteristics

The systematic review included 7 studies published between 2004-2024, comprising 5 in vitro studies[22-24,26,28] and 2 pre-clinical study[25,28] investigated different *Weissella* strains (*W. confusa*,

Table 2. Outcome of included studies

Study (Year)	Primary Outcomes	Measurement Method	Results (Mean ± SD, % and fold Change)	Secondary Outcomes
Lee[22]	Pathogen inhibition by interference assay and broth dilution	MPN Method	Growth inhibition of pathogens *C. albicans* (8%) and *E. coli* (38%) by broth dilution method	Adherence to T24 cells and coaggregation of *C. albicans* or *E. coli* with *W. confusa* PL9001
Lee[23]	*C. albicans, E. coli, S. aureus* and *S. agalactiae* inhibition to colonizing vaginal cells at different pH	pH meter Colony counting	No SD or percentage values mentioned	The number of adhered *W. kimchi* cells to vaginal cells increased at a lower pH
Thamacharoensuk et al.[24]	IL-12 induction	ELISA	IL-12 productivity ↑ (1585.23 ± 7.80 pg/mL)	↑ cell viability for *W. thailandensis* PC79-5 and *W. confusa* MSMC57-2 by 1.85% in acid bile conditions
Oh and Lee[25]	NK cell activation	Flow cytometry	No SD mentioned	JW15 increased intracellular cytolytic molecules, such as perforin, granzyme B, and IFN-γ
Amer et al.[26]	Antimicrobial effects	Diameter measurement	No SD mentioned	Anti-cancerous activity against MCF-7 (58%), reduction in DPPH at 39.8 µg /ml Nano crude EPS
Choi and Yun[28]	Anticancer activity of *W. cibaria*	Tumor volume measured	Reduced tumor volume by 2.4 times for CT26 and 16.3 times for MC38 compared to control	Composition can be used for the treatment or prevention of various cancer including uterine cancer
Lee et al.[29]	*C. albicans* biofilm reduction	Diameter measurement	Zone of Inhibition: 11.2 ± 0.3 mm	↓ *C. albicans* biofilm ($P < 0.001$).Inhibitory effect of pro-inflammatory cytokine production

W. cibaria, *W. kimchii*, *W. paramesenteroides*) with varying intervention protocols. Table 1 presents the features of the selected studies, while Table 2 highlights their main results. Overall complete information about the results of the study is mentioned in the Supplementary Material.

Microbiological outcomes in terms of pathogen inhibition were assessed in terms of adhesion reduction and biofilm disruption. For instance, *W. confusa* PL9001 decreased the number of adhered pathogens of *E. coli* (8.47%), *C. albicans* (11.54%), *S. aureus* (58.59%) and VRE (37.88%) to epithelial (T24) cells. In the study, *W. confusa* PL9001 modulated the vaginal microenvironment by inhibiting the growth of UTI pathogens by 38% of *E. coli* and 8% with *C. albicans.*[22] *W. kimchii* PL9023 produces hydrogen peroxide and bacteriocin like substances which can inhibit various pathogens associated with vaginal infections.[24] *W. confusa* WIKIM51 reduced *C. albicans* with the formation of zone of inhibition with the diameter of 11.2 ± 0.3 ($P < 0.001$).[28]

In the outcome of immunomodulatory effects, *Weissella* spp. increased IL-12 (highest in *W. cibaria* 1585.23 ± 7.80 pg/mL vs lowest in *L. paracasei* 430.65 ± 35.02 pg/mL).[24] *W. cibaria* WIKIM28 elevated IL-10 (320±45 pg/mL) while reducing TNF-α (110 ± 15 pg/mL vs 250 ± 30 control) ($P < 0.05$).[28] On the other hand, *W. cibaria* JW15 enhanced CD69+ NK cells.[25] Apart from these, both crude and pure nano-EPS produced from *W. paramesenteroides* MN2C2 has anti-cancer activity against various cancerous cell lines with highest activity of crude nano-EPS of 1.3 mg/ml (lowest IC_{50}) is recorded to have highest selective index of 6.9 against MCF-7.[26]

Risk of bias assessment

The risk of bias (RoB) was assessed to the seven studies retrieved, as displayed in Table 3 and Supplementary material. Two in vitro studies Lee et al. and Thamacharoensuk et al.[23,24] out of 5, have found some concerns (Cochrane RoB 2) due to unblinded design. On the other hand, two in

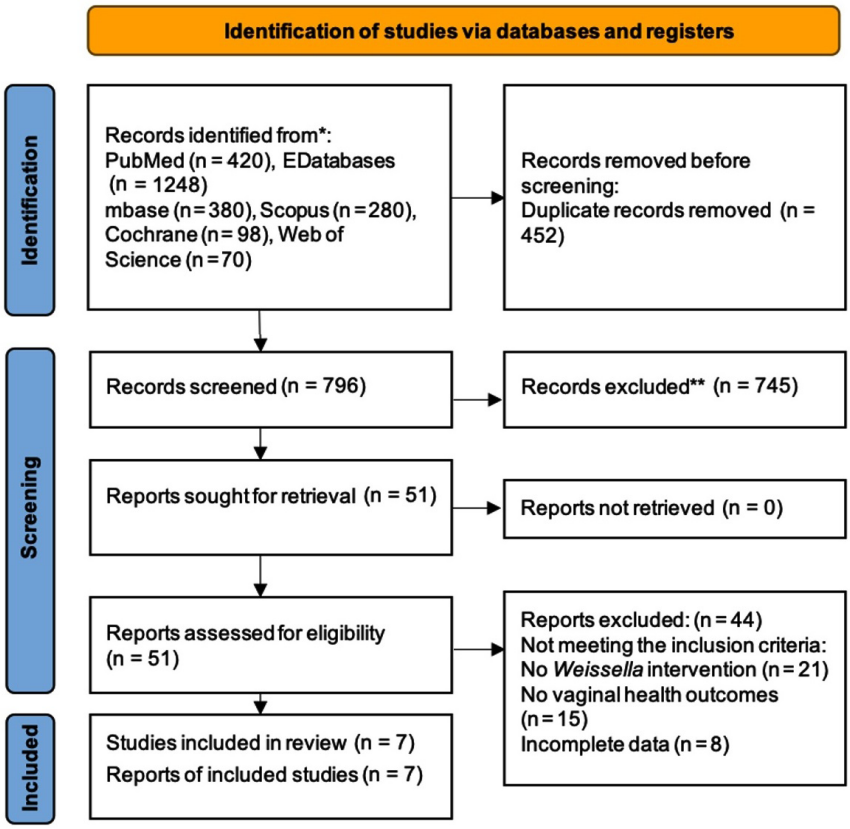


Figure. Workflow of the study selection process using PRISMA 2020

Table 3. Risk of bias

Study (Year)	Randomization	Blinding	Incomplete Data	Selective Reporting	Other Bias	Overall
Lee[22]	N/A	✗	✓	✓	! (No strain validation)	!
Lee[23]	N/A	✗	✓	✓	Performed in triplicates	✓
Thamacharoensuk[24]	N/A	✗	✓	✓	! (Single dose)	!
Oh and Lee[25]	N/A	✓	✓	✓	✓	✓
Amer et al.[26]	✗	✗	!	✗ (Patent)	✗ (Industry-funded)	✗
Choi and Yun[28]	✗	✗	✓	✗ (Patent)	✗	✗
Lee et al.[29]	N/A	✓	✓	✓	✓	✓

*(✓ = Low risk, ! = Some concerns, ✗ = High risk)

vitro studies Oh et al.[25] and Lee et al.[29] were marked as low risk than the other in vitro study.[21] Sterne et al.[26] and Choi et al.[28] were marked as High risk (SYRCLE) for industry-linked patents (Table 3).

We have also performed evidence quality on the retrieved studies. It was found that studies from 2021-2024 demonstrate improved methodological rigor (100% cell line validation vs 0% in 2004-2005) and broader outcome measures (biofilm + immunity/adhesion focus).

Study key findings include that strain-specific effects were observed in which *W. confusa* showed blockage of congregation of *C. albicans*, while *W. cibaria* had optimal immunomodulation. There is a dose-response gap in the overall studies, as only a single study tested multiple doses.[24] So, furthermore, clinical translation is needed.

While this systematic review identified promising evidence for *Weissella* probiotics in vaginal health across seven studies (2004-2024), quantitative synthesis through meta-analysis was not feasible due to significant methodological heterogeneity. The included studies varied substantially in design (five in vitro studies, and two pre-clinical studies), outcome measures (ranging from pathogen adhesion rates to cytokine levels), and model systems (cell cultures vs. pre-clinical trials). Outcomes like pH modulation or biofilm reduction were reported by single studies using incompatible methodologies. Additionally, incomplete reporting of standard deviations and varying *Weissella* strains (*W. confusa, W. cibaria, W. kimchii*) further precluded statistical pooling. Instead, a qualitative synthesis revealed consistent positive trends, with 100% of studies demonstrating beneficial effects in their respective outcome measures, particularly for *W. confusa's* anti-adhesion properties and *W. cibaria's* immunomodulation. The review highlights an urgent need for standardized clinical trials measuring comparable endpoints (e.g., Nugent scores across ≥3 studies) to enable future meta-analyses. Currently, the evidence supports narrative integration of mechanisms while underscoring the preliminary nature of these findings due to risk of bias concerns (two high-risk industry-linked studies). Researchers should prioritize replicating key outcomes like biofilm disruption in controlled clinical settings to permit quantitative synthesis.

DISCUSSION

Despite recently advanced treatment options for vaginal infections, the associated side effects such as loss of beneficial microflora, vaginal dryness, itching, occurrence of secondary infections, render the therapy less effective. Resistance to the standard antibiotics is a major growing concern during the treatment, thereby calling for development of new and effective alternative therapies. Probiotics have been extensively reported for their effect on maintaining normal vaginal flora and, thus promoting vaginal health. Recently, genus *Weissella* has emerged as a probiotic for their

potential role in promoting vaginal health. The present systematic review focuses on the role of different *Weissella* strains such as *W. confusa, W. kimchi, Weissella paramesenteroides* in promoting vaginal health. Lee[22] reported antimicrobial properties of clinical isolate *W. confusa* PL9001 against isolated uropathogens. Co-aggregation test also suggested that *W. confusa* PL9001 prevented adherence of these UTI pathogens. In the study by Lee,[23] isolated more than 100 LAB from vagina of healthy females, of which all *Weissella* spp. produced hydrogen peroxide with *W. kimchi* PL9023, producing significantly higher volumes of hydrogen peroxide. *Weissella* also produced lactic acid and bacteriocin-like substance along with hydrogen peroxide, which inhibited the growth of isolated vaginal pathogens *C. albicans*, *S. aureus*, *E. coli* and *Streptococcus agalactiae.* Lee et al.[29] investigated the antifungal activity of *W. confusa* WIKIM51 (Wilac D001) against *C. albicans*. The inhibitory effect was not only equivalent to *L. reuteri* and *L. rhamnosus,* but it also strongly downregulated the pro-inflammatory cytokines IL-6 and IL-8, which are otherwise increased during infection with *C. albicans*. Contrarily, the regulation of IL-6 and IL-8 by *L. reuteri* and *L. rhamnosus* was not significant.[29] Immune modulatory activity of kimchi probiotic *Weissella ciberia* has reported by Oh and Lee[25] which can play an important role in preventing cancer. Their findings indicated consumption of such probiotics will help to reduce inflammation and combat infections, which will enhance vaginal health. Thamacharoensuk et al.[24] found that out of all the studied LAB, *W. cibaria* PC86-2 significantly modulated the production of IL-12 and can prevent cancer by stimulating cell-mediated responses.[24] *Weissella paramesenteroides* MN2C2 isolated from buffalo colostrum was reported by Sterne et al.[26] This organism showed resistance to acidic environment and bile salt as well as to pancreatic enzymes. The antimicrobial properties of this bacteria were tested on various microorganisms such as *Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Streptococcus agalactiae, Aeromonas hydrophila,* and *Salmonella enterica.* In addition, exopolysaccharide derived nanoparticles synthesized from *Weissella paramesenteroides* MN2C2 were found to have inhibitory effect on MCF-7, Caco-2 and HepG-2 cells. Moreover, these nanoparticles also have antioxidant property. Their study implies that supplementation of probiotics, including *Weissella* spp., could increase quality of life in post-operative cancer patients. Choi and Yun[27] patented a pharmaceutical composition containing *Weissella cibaria* WIKIM28 for its anti-cancer properties. Additional *Weissella* strains that were not included in the present review have also been reported to possess potentially beneficial biological properties. Kwon et al.[30] did a pilot study to get insights into the impact of probiotic supplementation consisting of nine strains belonging to *Lactobacillus* and *Bifidobacterium* spp. in post-operative cancer patients. Their study implies that supplementation of probiotics, increased *Weissella* spp. along with other beneficial bacteria that could increase quality of life in post-operative cancer patients, suggesting the beneficial importance of *Weissella* spp. Park et al.[31] did a double blinded, randomized, placebo controlled clinical trials on consumption of *W. cibaria* CMS1 by 90 health individuals for 12 weeks. Data from the study revealed that consumption of *W. cibaria* CMS1 increased production of salivary immunoglobulin A (sIgA) while decreasing tumor necrosis factor alpha (TNF- α) significantly with P-value, $P = 0.046$ and $P = 0.008$ respectively. Their study not reported increase in presence of *Lactobacillales*, Bacilli, and *Streptococcaceae* but also reported beta diversity change in oral microbiota by increasing abundance of *Furmicutes* and *Acinetobacter* and decreasing abundance of Bacteroidetes and Fusobacteria after consumption of *W. cibaria* for 12 weeks. Similarly, probiotic intervention of specific *Weissella* strain might also increase the abundance of beneficial microbes and modulate immune response in vagina and enhance vaginal health.[31] The probiotic potential of the vaginal strain *Weissella confusa* MV0113 was assessed based on genomic analysis, in vitro and pre-clinical studies by Luo et al.[32] The cell free supernatant of the *Weissella confusa* MV0113 strain inhibited the biofilm formation of *Candida albicans* and *Gardnerella vaginalis*. In animal models, the administration of *Weissella confusa* MV0113 resulted in modulations in inflammation responses and the restoration of beneficial *Lactobacillus* strains. *Weissella paramesenteroides* UFTM 2.6.1, a bacterial isolate isolated from bovine milk, showed *anti-Listeria* activity via in

silico and in vitro studies.[33] Further, in another study, omics-based analysis of the strain *Weissella confusa* UTNCys2-2 indicated that the bacterial strain can synthesize exopolysaccharides and other bioactive metabolites.[7,34] Moreover, the cell free supernatant of *Weissella confusa* K3 exerted antibacterial effect against uropathogenic bacteria producing extended spectrum β-lactamases.[35] However, information on the activity of the aforementioned strains against vaginal pathogens is not available yet.

The present review summarizes the potential probiotic role of *Weissella* spp. that could improve vaginal health in women by inhibiting adherence and growth of pathogens, immunomodulating cytokines levels, activating NK cells activity, enhancing antioxidant and anticancer properties. However, further large-scale clinical studies are warranted to strengthen the potential of *Weissella* spp. as promoters of vaginal health in women. Moreover, specific strains, route of administration, optimal dosage, and treatment duration need to be carefully standardized for *Weissella* spp. to make it a commercial probiotic in the future.

Strengths and limitations

Strengths

To ensure that all relevant research studies could be located, searching was done using several databases and sources, including those in various languages.

Rigorous methodology adhering to PRISMA guidelines with dual independent review at all stages.

Detailed quality assessment using appropriate tools for different study designs.

Transparent reporting through protocol registration and full disclosure of methods.

Limitations

1. Heterogeneity in *Weissella* strains, formulations, and outcome measures.
2. Limited long-term data with most included studies having short follow-up periods.
3. Potential publication bias with possible underrepresentation of negative results.
4. Mechanistic focus of some included studies creating uncertain clinical relevance.
5. No clinical studies obtained where *Weissella* spp. were used as an intervention.
6. Language bias with most evidence available in English despite no language restrictions.

This methodology ensured a systematic, transparent, and reproducible synthesis of evidence regarding *Weissella* probiotics for vaginal health. The approach balanced comprehensiveness with feasibility, employing appropriate tools for quality assessment and data synthesis. These methods minimized bias while providing meaningful conclusions to inform both clinical practice and future research directions.

CONCLUSION

Weissella spp. offers a promising potential in ameliorating vaginal health in women, particularly in managing conditions such as bacterial vaginosis, candidiasis, and possibly even cancer. Yet, human trials have to be carried out to determine clinical significance through safety, effectiveness, and impacts of *Weissella* formulations, which will involve randomized control trials. Furthermore, strain-specific characteristics and mechanisms of action need to be studied for prospective clinical application.

SUPPLEMENTARY INFORMATION

Supplementary information accompanies this article at https://doi.org/10.22207/JPAM.20.4.26

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

RKG conceptualized the study. VV designed the study. MB, SP and AJ performed investigation. MB, VV and AJ performed data analysis. AJ and RKG supervised the study. SP and MB wrote the manuscript. AJ, VV and RKG revised

the manuscript. All authors read and approved the final manuscript for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript and/or in the supplementary files.

ETHICS STATEMENT

Not applicable.

REFERENCES

1. Pendharkar S, Skafte-Holm A, Simsek G, Haahr T. Lactobacilli and their probiotic effects in the vagina of reproductive age women. *Microorganisms*. 2023;11(3):636 doi: 10.3390/microorganisms11030636
2. Al-Yami AM, Al-Mousa AT, Al-Otaibi SA, Khalifa AY. *Lactobacillus* species as probiotic: isolation sources and health benefits. *J Pure Appl Microbiol*. 2022;16(4):2270-2291. doi: 10.22207/JPAM.16.4.19
3. Waziri A, Bharti C, Aslam M, et al. Probiotics for the chemoprotective role against the toxic effect of cancer chemotherapy. *Anti-Cancer Agents Med Chem.* 2022;22(4):654-667. doi: 10.2174/1871520621666210514000615
4. Purkayastha SD, Bhattacharya MK, Prasad HK, et al. Probiotic and cytotoxic potential of vaginal *Lactobacillus* isolated from healthy northeast Indian women. *J Pure Appl Microbiol*. 2020;14(1): 205-214. doi: 10.22207/JPAM.14.1.22
5. Du Y, Liu L, Yan W, et al. The anticancer mechanisms of exopolysaccharide from *Weissella cibaria* D-2 on colorectal cancer via apoptosis induction. *Sci Rep.* 2023;13(1):21117 doi: 10.1038/s41598-023-47943-7
6. Khider M, El-Readi MZ, Abdalrahim S, et al. Functional low-fat set yogurt enhanced with microbial exo-polysaccharides-mediated anticancer activity. *J Pure Appl Microbiol*. 2022;16(4):2601-2618. doi: 10.22207/JPAM.16.4.28
7. Bochgire M, Pingale S, Kaul-Ghanekar R, Angadi K, Jadhav A. *Weissella*: A multifaceted genus making the way for next-gen biotherapeutics? *Antonie van Leeuwenhoek.* 2026;119(5):96. doi: 10.1007/s10482-026-02307-9
8. Li YQ, Tian WL, Gu CT. *Weissella sagaensis* sp. nov., isolated from traditional Chinese yogurt. *Int J Syst Evol Microbiol.* 2020;70(4):2485-2492 doi: 10.1099/ijsem.0.004062
9. Yadav M, Sunita, Shukla P. Probiotic potential of *Weissella paramesenteroides* MYPS5.1 isolated from customary dairy products and its therapeutic application. *3 Biotech*. 2022;12(1):9. doi: 10.1007/s13205-021-03074-2
10. Padonou SW, Schillinger U, Nielsen DS, et al. *Weissella beninensis* sp. nov., a motile lactic acid bacterium from submerged cassava fermentations, and emended description of the genus *Weissella*. *Int J Syst Evol Microbiol.* 2010;60(Pt 9):2193-2198. doi: 10.1099/ijs.0.014332-0
11. Snauwaert I, Papalexandratou Z, De Vuyst L, Vandamme P. Characterization of strains of W*eissella fabalis* sp. nov. and *Fructobacillus tropaeoli* from spontaneous cocoa bean fermentations. *Int J Syst Evol Microbiol.* 2013;63(Pt 5):1709-1716 doi: 10.1099/ijs.0.040311-0
12. Wouters D, Grosu-Tudor S, Zamfir M, De Vuyst L. Bacterial community dynamics, lactic acid bacteria species diversity and metabolite kinetics of traditional Romanian vegetable fermentations. *J Sci Food Agric.* 2013;93(4):749-60 doi: 10.1002/jsfa.5788
13. Nisiotou A, Dourou D, Filippousi ME, Banilas G, Tassou C. *Weissella uvarum* sp. nov., isolated from wine grapes. *Int J Syst Evol Microbiol.* 2014;64(Pt_11):3885-3890 doi: 10.1099/ijs.0.066209-0
14. Lakra AK, Domdi L, Hanjon G, Tilwani YM, Arul V. Some probiotic potential of *Weissella confusa* MD1 and *Weissella confusa* MD2 isolated from fermented batter. *Lwt.* 2020;125. doi: 10.1016/j.lwt.2020.109261
15. Mun SY, Chang HC. Characterization of *Weissella koreensis* SK isolated from kimchi fermented at low temperature (around 0 °C) based on complete genome sequence and corresponding phenotype. *Microorganisms*. 2020;8(8):1147 doi: 10.3390/microorganisms8081147
16. Suwannaphan S. Isolation, identification and potential probiotic characterization of lactic acid bacteria from Thai traditional fermented food. *AIMS Microbiol.* 2021;7(4):431-446. doi: 10.3934/microbiol.2021026
17. Praet J, Meeus I, Cnockaert M, Houf K, Smagghe G, Vandamme P. Novel lactic acid bacteria isolated from the bumble bee gut: *Convivina intestini* gen. nov., sp. nov., *Lactobacillus bombicola* sp. nov., and *Weissella bombi* sp. nov. *Antonie van Leeuwenhoek.* 2015;107(5):1337-49. doi: 10.1007/s10482-015-0429-z
18. Heo J, Hamada M, Cho H, et al. *Weissella cryptocerci* sp. nov., isolated from gut of the insect *Cryptocercus kyebangensis. Int J Syst Evol Microbiol.* 2019;69(9):2801-2806. doi: 10.1099/ijsem.0.003564
19. Lin ST, Wang LT, Wu YC. *Weissella muntiaci* sp. nov., isolated from faeces of Formosan barking deer (*Muntiacus reevesi*). *Int J Syst Evol Microbiol.* 2020;70(3):1578-1584 doi: 10.1099/ijsem.0.003937
20. Pereira FL, Dorella FA, Castrejon-Najera J, et al. Comparative polyphasic characterization of *Weissella* strains isolated from beaked whale and rainbow trout (Oncorhynchus mykiss): confirmation of *Weissella ceti* sp. nov. and description of the novel *Weissella tructae* sp. nov. isolated from farmed rainbow trout. *Braz J Microbiol.* 2022;53(4):2263-2272 doi: 10.1007/s42770-022-00856-5
21. Joglekar A, Nimonkar Y, Bajaj A, Prakash O. Resolution of inter/intraspecies variation in *Weissella* group requires multigene analysis and functional characterisation. *J Basic Microbiol.* 2023;63(2):140-155. doi: 10.1002/jobm.202200357
22. Lee, YH. *Weissella confusa* strain PL9001 inhibits

growth and adherence of genitourinary pathogens. *J Microbiol Biotechnol.* 2004;14(4):680-685.

23. Lee Y. Characterization of *Weissella kimchii* PL9023 as a potential probiotic for women. *FEMS Microbiol Lett.* 2005;250(1):157-162. doi: 10.1016/j.femsle.2005.07.009
24. Thamacharoensuk T, Taweechotipatr M, Kajikawa A, Okada S, Tanasupawat S. Induction of cellular immunity interleukin-12, antiproliferative effect, and related probiotic properties of lactic acid bacteria isolated in Thailand. *Ann Microbiol.* 2017;67:511-518. doi: 10.1007/s13213-017-1280-4
25. Oh EY, Lee SM. Natural killer cell activation by *Weissella cibaria* JW15 isolated from Kimchi*. J Bacteriol Virol.* 2021;51(2):62-73 doi: 10.4167/jbv.2021.51.2.062
26. Sterne JA, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:14898. doi: 10.1136/bmj.l4898
27. Amer M, Eldiwany A, Elgammal E, Atwa N, Dawoud I, Rashad F. Nano-exopolysaccharide from the probiotic *Weissella paramesenteroides* MN2C2: production, characterization and anticancer activity. *Egypt J Chem.* 2021;64:7023-7033 doi: 10.21608/ejchem.2021.81338.4031
28. Choi HJ, Yun MS. Pharmaceutical composition for publication classification preventing or treating cancer, comprising *Weissella cibaria* wikim28 as active ingredient. 2022:EP3895717B1
29. Lee G, You YA, Ansari A, et al. The antifungal effect of *Weissella confusa* WIKIM51 (Wilac D001) on vaginal epithelial cells infected by *Candida albicans*. *Appl Sci.* 2024;14(7):2676. doi: 10.3390/app14072676
30. Kwon H, Chae SH, Jung HJ, et al. The effect of probiotics supplementation in postoperative cancer patients: A prospective pilot study. *Ann Surg Treat Res.* 2021;101(5):281-290. doi: 10.4174/astr.2021.101.5.281
31. Park MJ, Park S, Kim KJ, Oh B, Kim JY. Effect of the probiotic *Weissella cibaria* CMS1 on the immune response and the oral microbiome: a randomized, double-blind, placebo-controlled, parallel study. *Food Funct.* 2024;15(8):4409–4420. doi: 10.1039/d4fo00195h
32. Luo C, Dong X, Song J et al. Vaginal *Weissella confusa* MV0113 suppresses pathogens and restores microbiota to alleviate bacterial vaginosis: integrated genomic and in vivo evidence. *BMC Microbiol*. 2025;26(1):51. doi: 10.1186/s12866-025-04552-w
33. Rocha BM, Sabino YN, de Almeida TC et al. Unlocking probiotic potential: genomic insights into *Weissella paramesenteroides* UFTM 2.6. 1. *Probiotics & Antimicro Prot.* 2025;17(6):4764-4777. doi: 10.1007/s12602-024-10409-x
34. Tenea GN. Comprehensive genomic and metabolomic profiling of *Weissella confusa* UTNCys2-2 highlights bioactive potential. *Front Microbiol.* 2026;17:1779198. doi: 10.3389/fmicb.2026.1779198
35. El-Mekkawy RM, Hamour NE, Hassanein WA, Allam AA. Evaluation of the antibacterial activity of *Weissella confusa* K3 cell-free supernatant against extended-spectrum βeta lactamase (ESBL) producing uropathogenic *Escherichia coli* U60. *Saudi J Biol Sci*. 2023;30(4):103595. doi: 10.1016/j.sjbs.2023.103595