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Review Article

Efficacy of probiotic Lactobacillus reuteri on chronic generalised periodontitis: A systematic review of randomized controlled clinical trials in humans

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ABSTRACT

Background: It is well recognized fact that periodontal diseases are caused by multifactorial etiologies; in which microorganisms play an important role. An essential component of therapy is to eliminate or manage these pathogens. This has been traditionally accomplished through mechanical means by scaling and root planning and adjunctive anti-infective therapy, which includes local and systemic antimicrobials. But the unwarranted use of antimicrobial is associated with adverse effects and development of resistance. To overcome these problems newer technologies have been tested in the field of periodontics; one of these therapies is use of probiotic. This approach of therapy is of interest to periodontist due to the aforementioned shortcomings of conventional methods.

Materials and Methods: A manual and electronic search was made for human studies up to November 2020 that presented systemic and local use of probiotics in generalised chronic periodontitis. A systematic approach was followed by two independent reviewers and included eligibility criteria for study inclusion, quality assessment, and determination of outcome measures, data extraction, data synthesis, and drawing of conclusion.

Results: Only 3 randomized controlled human trials qualified, and they concluded that use of probiotic Lactobacillus Reuteri proves beneficial in improving clinical and microbiological parameters in generalised chronic periodontitis.

1. Introduction

The dietary use of living microorganisms has a long history. Mention of cultured dairy products is found in the bible and the sacred books of Hinduism. Probiotics have been used for decades in fermented products, but potential use of probiotics as a nutritional medical therapy has not been formally acknowledged. Going back to history of probiotics;In 1907 the Ukrainian-born biologist and Nobel laureate Metchnikoff observed that bacteria in the fermented milk competed with the micro-organisms that are injurious to health, he discovered Lactobacillus bulgaricus and developed a theory that lactic acid bacteria (present in Bulgarian yoghurt) in the gastrointestinal tract could, by preventing putrefaction, prolong life. The concept of probiotics was thus born.[1] The term probiotic, meaning "for life," is derived from the Greek language. It was first used by Lilly and Stillwell in 1965 to describe "one microorganism which stimulates the growth of another" and thus was contrasted with the term antibiotic. In 1989, Fuller defined them as a live microbial food supplement, which beneficially affects the host animal by improving its microbial balance.[2] The first probiotic species introduced into research were Lactobacillus acidophilus by Hull, et al.

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in 1984.[3] Probiotics are described as live micro-organisms which when administered in adequate numbers confer a health benefit on the host (FAO/WHO 2001).[4]

Gibson and Roberfroid exchanged "pro" for "pre" in the word, Probiotics, which means "before" or "for". They defined prebiotics as a "non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon. The term symbiotic is used when a product contains both probiotics and prebiotics.[5] In 1994, the World Health Organization supposed probiotics to be the next-most important immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. These incidences flagged a way for a new notion of probiotics in medicine and dentistry. Thus the purpose of this systematic review is to discuss the beneficial role of probiotic lactobacillus reuteri in generalised chronic periodontitis.

2. Materials and Methods

2.1. Rationale

This systematic review evaluates literature based evidence in an effort to determine the efficacy of currently available probiotics, in controlling pathogenic micro flora involved in generalized chronic periodontitis.

2.2. Focused question

The question addressed in this systematic review was: "In patients with generalized chronic periodontitis, what are the effects of probiotics Lactobacillus reuteri on clinical and microbiological parameters?"

2.3. Search protocol

2.3.1. Data sources and search strategies

A search of MEDLINE, the Cochrane central trials register, and web of science was conducted up to November 2020. The review and all associated searches were confined to studies published in English language. The MEDLINE and Cochrane Library database were searched from 1950 till November 2020 using the following Medical subject headings (MeSH): probiotics, prebiotics, Lactobacillus returi. Following completion of MEDLINE and Cochrane controlled trials registry searches, a supplementary search was conducted in each of this database to include use of probiotics in generalised chronic periodontitis to assure consistency with the study protocol.

A total of 34 studies were identified addressing the use of probiotics in different forms of periodontitis, in vitro studies and animal studies. The studies were examined by 2independent reviewers (AA and VA) to select studies relevant to the specific question posed in this systematic review. Based on the study titles and abstracts, we selected 3 studies which fulfilled the inclusion criteria.

2.3.2. Probiotics v/s Replacement therapy

The possible use of antagonistic organisms to control pathogens and prevent disease is called as replacement therapy. There are two mail approaches by which replacement therapy can be rendered to enhance colonization resistance 1. Plaque preemptive colonization 2. Competitive displacement.[6]Replacement therapy can also be called as periodontal pocket recolonization, The concept of bacterial replacement therapy in periodontics was first introduced by Teughels et al in 2007. They reported that the subgingival application of a bacterial mixture including Streptococcus sanguis, S. salivarius, and Streptococcus mitis after scaling and root planing significantly suppressed the recolonization of Porphyromonas gulae (canine P. gingivalis) and P. intermedia in a beagle dog model.[7] In replacement therapy, the effector strain is directly applied on the site of infection and colonization of the site is essential, but probiotics are generally used as a dietary supplements, they exert a beneficial effect without colonization of the site.

2.3.3. Mechanisms of action of Probiotics/prebiotics

The mechanism of action vary according to the specific strain or combinations of strains used, the presence of prebiotics and the condition that is being treated, as well as the stage of the disease process in which the probiotic is administered. There are common themes emerging in studies of the modes of action of probiotics and numerous mechanisms have been proposed including: Inhibition of pathogen adhesion, colonization and biofilm formation, Induction of expression of cytoprotective proteins on host cell surfaces, Inhibition of collagenases and reduction of inflammation associated molecules, Stimulation and modulation of the host immune system, e.g. by reducing production of proinflammatory cytokines through actions on NFκB pathways, increasing production of anti-inflammatory cytokines such as IL-10, Modulation of cell proliferation and apoptosis eg. Prevention of cytokine induced apoptosis, Killing or inhibition of growth of pathogens through production of bacteriocins or other products, such as acid or peroxide, which are antagonistic towards pathogenic bacteria, Probiotics can also modify the surrounding environment by modulating the pH and/or the oxidation–reduction potential, which may compromise the ability of pathogens to become established.[8,9] Aggregation alteration is another important proposed mechanics as Hetrofermentative Lactobacillus is the strongest inhibitor of Aggregatibacter actinomycetemcomitans, Porphyromonasm gingivalis and Prevotella intermedia.[10]

Table 1: Probiotics in periodontal diseases: Human studies: n=7

S.No.	Name of the author/year	Study design	Type of study/ type of probiotic	Results	Conclusion
1	Teughels W et al 2013 [11] Lactobacillus reuteri-containing probiotic lozenges as an adjunct to scaling and root planing (SRP).	30 chronic periodontitis patients were recruited and monitored clinically and microbiologically at baseline, 3, 6, 9 and 12 weeks after therapy. All patients received one-stage full-mouth disinfection and randomly assigned over a test (SRP + probiotic, n = 15) or control (SRP + placebo, n = 15) group. The lozenges were used two times a day for 12 weeks	Randomized placebo-controlled clinical trial/ Lactobacillus reuteri Lozenges	At week 12, all clinical parameters were significantly reduced in both groups, while there was significantly more pocket depth reduction ($p < 0.05$) and attachment gain ($p < 0.05$) in moderate and deep pockets; more Porphyromonasgingivalis reduction was observed in the SRP + probiotic group.	The results indicate that oral administration of L. reuteri lozenges could be a useful adjunct to SRP in chronic periodontitis.
2	Shah MP et al 2013 [12] Evaluation of the effect of probiotic (inersan®) alone, combination of probiotic with doxycycline and doxycycline alone on aggressive periodontitis	30 patients, who satisfied the inclusion and exclusion criteria, were assigned to one of the above mentioned three groups by using block randomization. The clinical and the microbiological parameters were recorded on day 0, at 2 weeks and at 2 months. On day 0, before recording the clinical parameters, 0.5 ml of unstimulated saliva was collected for the evaluation of the microbiological parameters. The clinical parameters which were recorded were the plaque index, the gingival index, the probing pocket depth and the clinical attachment level. The microbiological parameters which were recorded were Lactobacilli and Aggregatibacter actinomycetemcomitans. After this, Scaling and Root Planing (SRP) was performed on day 0. Two weeks after the SRP, the patients were recalled for the saliva sample collection and for the evaluation of the clinical parameters. On the same day, medications were given to the patients to be taken for fourteen days according to the group which they belonged to (Group A - probiotic alone, Group B - a combination of the probiotic with doxycycline, Group C - doxycycline alone). The patients were then recalled at two months for the saliva sample collection and for the evaluation of the clinical parameters	Clinical and microbiological study/lactobacillus brevis [inersan] CD2 Tablet	The administration of the probiotic alone, a combination of the probiotic with doxycycline and doxycycline alone, resulted in a decrease in the plaque index, the gingival index, the probing pocket depth and the clinical attachment level at 2 months, which was statistically significant ($p < 0.05$). The A. actinomycetemcomitans count tended to decrease in all the three groups at 2 months, which was statistically non-significant ($p > 0.05$). The Lactobacilli count tended to increase significantly in the probiotic alone group ($p < 0.05$).	As an alternative to antibiotics, probiotics can be used, as they repopulate the beneficial microflora and reduce the pathogenic bacteria.

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Table 1 continued

3	Vicario M et al 2013[13] Clinical changes in periodontal subjects with the probiotic Lactobacillus reuteriProdentis	Twenty systemically healthy, non-smoking subjects with initial-to-moderate chronic periodontitis were enrolled in this 1-month double-blind, placebo-controlled, randomized clinical trial. Subjects were randomly assigned to receive tablets containing Lactobacillus reuteriProdentis or placebo once a day for 30 days. Clinical parameters were collected at baseline and 30 days post-treatment.	Preliminary randomized clinical trial/ Lactobacillus reuteri Tablet	Periodontal clinical parameters were improved in the test group after a 30-day intervention. The test group demonstrated a statistically significant reduction ($p < 0.05$) in all the periodontal parameters included in the study (plaque index, bleeding on probing and pocket probing depths), while the control group treated with placebo did not show any statistically significant change in periodontal parameters.	These data indicate that oral administration of Lactobacillus reuteri Prodentis improved the short-term clinical outcomes in non-smoking patients with initial-to-moderate chronic periodontitis.
4	Iwamoto T et al 2010[14] Effects of probiotic Lactobacillus salivarius WB21 on halitosis and oral health	Twenty patients with genuine halitosis were given 2.0 x 10(9) Lactobacillus salivarius WB21 and xylitol in tablet form daily. Oral malodor and clinical parameters were evaluated at the same time of day for each patient after 2 and 4 weeks	An open-label pilot trial./ Lactobacillus salivarius WB21 Tablet	All 20 patients were positive for L. salivarius DNA in their saliva at 2 weeks, although 12 patients were negative for this organism at baseline. Oral malodor parameters significantly decreased at 2 weeks in the subjects with physiologic halitosis. The scores of an organoleptic test and bleeding on probing significantly decreased at 4 weeks in the subjects with oral pathologic halitosis.	Oral administration of probiotic lactobacilli primarily improved physiologic halitosis and also showed beneficial effects on bleeding on probing from the periodontal pocket.

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Table 1 continued

5	Vivekananda MRet al 2010[15] Effect of the probiotic Lactobacilli reuteri (Prodentis) in the management of periodontal disease	Thirty, otherwise systemically healthy, chronic periodontitis patients (19 males and 11 females, aged between 34 and 50 years) were included. The study period was 42 days. 'Split-mouth' design was used for the SRP, which was performed on day 0; two quadrants (either right or left) were treated with SRP whereas the remaining two quadrants were left untreated. The participants received a toothbrush, toothpaste, and brushing instructions. L. reuteriProdentis lozenges (1×10(8) CFU DSM17938+1×10(8) CFU ATCC PTA 5289) or the corresponding placebo lozenges were taken twice daily from day 21 to day 42. Statistical analysis was done for comparisons of clinical parameters (Plaque Index (PI), Gingival Index (GI), Gingival Bleeding Index (GBI), probing pocket depth (PPD), clinical attachment level (CAL)) and microbiological levels of the pathogens Aggregibactera- ctinomycetemcomitans (Aa), Porphyromonasgingivalis (Pg), and Prevotellaintermedia (Pi). All p-values less than 0.05 were considered significant. Assessments were made on day 0 before SRP treatment, on day 21 before administration of the lozenges, and on day 42.	A preliminary randomized clinical trial./ Lactobacilli reuteri	At day 42, the PI, GI, and GBI were significantly reduced by all treatment modalities. When ranked, the amount of PI, GI and GBI reduction by the different treatments was SRP + ProdentisProdentis SRP + placebo placebo; all differences were statistically significant. For PPD and CAL, the best result was obtained with the SRP+Prodentis treatment. PPD was reduced from 5.08±0.75 to 3.78±0.61 mm ($p<0.001$) and CAL from 3.93±0.93 to 2.85±0.74 mm ($p<0.001$). Prodentis, either alone or following SRP, reduced Aa, Pi, and Pg by 1 log(10) unit ($p<0.01$). The SRP+placebo combination did not significantly affect the levels of the pathogens.	The present randomized controlled trial confirms the plaque inhibition, anti-inflammatory, and antimicrobial effects of L. reuteriProdentis. L. reuteriProdentis probiotic can be recommended during non-surgical therapy and the maintenance phase of periodontal treatment.

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Table 1 continued

6	Mayanagi G et al 2009 [16] Probiotic effects of orally administered Lactobacillus salivarius WB21-containing tablets on periodontopathic bacteria	Sixty-six healthy volunteers without severe periodontitis were randomized into two groups to receive lactobacilli or placebo for 8 weeks (8W): the test group (n=34) received 2.01 x 10(9) CFU/day of Lactobacillus salivarius WB21 and xylitol in tablets; the control group (n=32) received placebo with xylitol. Supra/subgingival plaque samples were collected at the baseline and after 4 weeks (4W) and 8W. The bacterial amounts in plaque samples were analysed by quantitative real-time polymerase chain reaction.	A double-blinded, placebo-controlled, randomized clinical trial./ Lactobacillus salivarius WB21	The numerical sum of five selected periodontopathic bacteria in the test group was decreased significantly in subgingival plaque at 4W [odds ratio (OR)=3.13, 95% confidence intervals (CI)=1.28-7.65, p=0.012]. Multivariate analysis showed that significantly higher odds were obtained for the reduction of Tannerella forsythia in subgingival plaque of the test group at both 4W (OR=6.69, 95% CI=2.51-17.9, p<0.001) and 8W (OR=3.67, 95% CI=1.45-9.26, p=0.006	Oral administration of probiotic lactobacilli reduced the numerical sum of five selected periodontopathic bacteria and could contribute to the beneficial effects on periodontal conditions
7	Shimauchi H et al 2008 [17] Improvement of periodontal condition by probiotics with Lactobacillus salivarius WB21	Freeze-dried Lactobacillus salivarius WB21 -containing tablets or a placebo were given to volunteers in a double-blind randomized study. A total of 66 volunteers were finally enrolled and randomly assigned to receive tablets containing WB21 (6.7 x 10(8) CFU) with xylitol or xylitol alone (placebo) three times a day for 8 weeks. Periodontal clinical parameters and whole saliva samples were obtained at baseline (BL), 4 weeks, and the end of the interventional period (8 weeks). Salivary lactoferrin (Lf) levels were measured by enzyme-linked immunosorbent assay. Lactobacilli in saliva and plaque samples was detected by semi-quantitative RT-PCR using 16S rRNA primers.	A randomized, double-blind, placebo-controlled study/ Lactobacillus salivarius WB21	Periodontal clinical parameters were improved in both groups after an 8-week intervention. Current smokers in the test group showed a significantly greater improvement of plaque index and probing pocket depth from BL when compared with those in the placebo group. Salivary Lf level was also significantly decreased in the test group smokers.	Our results indicate that probiotics could be useful in the improvement/maintenance of oral health in subjects at a high risk of periodontal disease.

Table 2: In vitro- studies: n=3

S.No.	Name of the Author/year	Study design	Type of study/ type of probiotic	Results	Conclusion
1	Chen LJ et al 2012 [18]	The antagonistic growth effects of Lactobacillus salivarius and Lactobacillus fermentum as well as their fermentative broth were thus tested using both disc agar diffusion test and broth dilution method, and their effects on periodontal pathogens, including Streptococcus mutans, Streptococcus sanguis, and Porphyromonasgingivalis in vitro at different concentrations and for different time periods were also compared.	In vitro/ Lactobacillus salivarius and Lactobacillus fermentum	Lactobacillus salivarius and Lactobacillus fermentum and their concentrated fermentative broth were shown to inhibit significantly the growth of Streptococcus mutans, Streptococcus sanguis, and Porphyromonasgingivalis, although different inhibitory effects were observed for different pathogens. The higher the counts of lactobacilli and the higher the folds of concentrated fermentative broth, the stronger the inhibitory effects are observed. The inhibitory effect is demonstrated to be dose-dependent. Moreover, for the lactobacilli themselves, Lactobacillus fermentum showed stronger inhibitory effects than Lactobacillus salivarius.	These data suggested that Lactobacilli and their fermentative broth exhibit antagonistic growth activity, and consumption of probiotics or their broth containing lactobacilli may benefit oral health.

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Table 2 continued

2	Saha S et al 2013 [19]	Novel carboxymethyl cellulose, Oral thin films CMC-OTFs were developed with varying CMC concentration (1.25 - 10 mg/mL), weight (5 - 40 g), thickness (16 - 262 μm), hygroscopicity (30.8 - 78.9 mg/cm(2) film), and dissolving time (135 - 600 s). The 10 g 5 mg/mL CMC-OTF was selected and used to incorporate Lactobacillus fermentum NCIMB 5221 (6.75 $\times$ 10(8) cells/film), a probiotic with anti-inflammatory potential for periodontitis treatment and capable of inhibiting microorganisms responsible for dental caries and oral candidiasis.	In vitro	The CMC-OTF maintained probiotic viability and antioxidant activity following 150 days of storage with a production of 549.52 ± 26.08 μMTrolox equivalents.	
3	Teanpaisan R et al 2011 [20]	Total 357 strains comprising 10 species of oral Lactobacillus, Lactobacillus fermentum (195), Lactobacillus salivarius (53), Lactobacillus casei (20), Lactobacillus gasseri (18), Lactobacillus rhamnosus (14), Lactobacillus paracasei (12), Lactobacillus mucosae (12), Lactobacillus oris (12), Lactobacillus plantarum (11) and Lactobacillus vaginalis (10) were used as producer strains. Inhibitory effect against a panel of indicators, periodontitis- and caries-related pathogens, was assessed	In vitro	The results have shown that oral Lactobacillus SD1-SD6 showed a strong inhibitory effect against Strep. mutans and Streptococcus sobrinus, as well as, Gram-negative periodontal pathogens Porphyromonas gingivalis and Aggregatibacteractinomycetemcomitans.	The results indicated that Lactobacillus may be of benefit as probiotics for the prevention of oral diseases.

Table 3: Animal studies: n=2

1	Messora MR et al 2013 [21]	Thirty-two rats were randomly divided into four groups: control (C), LIP, PROB [PROBIOTIC], and LIP/PROB. In groups PROB and LIP/PROB, the PROB was administered orally by addition to the drinking water of the animals for 44 days. In groups LIP and LIP/PROB, the mandibular right first molar of the animals received a cotton ligature that was left in the same position for 14 days. All animals were euthanized 44 days after the start of the PROB supplementation. The jaws were resected and histomorphometric analyses were performed. The measurements included evaluation of attachment loss (AL) and alveolar bone level (ABL) on the distal root of the mandibular first molar. Samples of the duodenum, jejunum, and ileum were also dissected from each animal to evaluate the villous height (VH) and crypt depth (CD). The data obtained were subjected to statistical analyses (analysis of variance, Tukey; $P < 0.05$).	In rats with ligature-induced periodontitis.[LIP]	Mean values of AL and ABL were significantly higher in group LIP compared with group LIP/PROB (AL: 3.05 ± 0.57 mm and 1.78 ± 0.63 mm, respectively; ABL: 4.21 ± 0.42 mm and 3.38 ± 0.17 mm, respectively). In group LIP/PROB, the mean values of VH and CD of the jejunum were significantly higher than the ones from group LIP (VH: 672.1 ± 83.3 μm and 528.0 ± 51.7 μm, respectively; CD: 463.8 ± 100.9 μm and 269.0 ± 48.4 μm, respectively	It can be concluded that PROB supplementation 1) reduces AL and alveolar bone loss in rats with LIP and 2) can protect the small intestine from reactive changes induced by LIP.

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Table 3 continued

2	Nackaerts O et al 2008[22]	Eight male beagle dogs with moderate periodontitis were enrolled in this split-mouth, double-blind randomized trial with ethical approval. Periodontal defects were surgically created bilaterally in the lower jaw. Four months later, the defects were randomly assigned to initial therapy (scaling and root planing) alone (control sites), or combined with multiple subgingival application of beneficial species. Intra-oral follow-up radiography was performed at this stage and 3 months later to verify the treatment effect.	Pilot radiographic evaluation in a dog model.	The bone density within periodontal pockets treated with beneficial bacteria improved significantly after 12 weeks, while this was non-significant for the control pockets, receiving a single root planing at baseline. There was a significant increase in the bone level at the end of the study for the pockets receiving beneficial bacteria. Again, no significance was noted for the control pockets.	This pilot study indicates the potential effect of a subgingival application of beneficial species in periodontal pockets, and illustrates the strength of standardized follow-up radiography to evaluate the effects of different treatment strategies on bone re-modelling.

The major mechanism of action of prebiotics is assumed to be indirect, i.e. facilitating the proliferation of beneficial components of the resident microflora prebiotics also exert direct effects on the host; independent of their effects on resident bacterial populations. These include stimulation of expression of IL-10 and interferon γ, enhancement of IgA secretion, modulation of inflammatory responses to pathogens.[23]

Probiotic Strains: The most common probiotic strains belong to the genera Lactobacillus and Bifidobacterium. Lactobacillus species from which probiotic strains have been isolated include L. acidophilus, L. johnsonii, L. casei, L. rhamnosus, L. gasseri, and L. reuteri. Similarly, the bifidobacterium strains include B. bifidum, B. longum, and B. infantis. Lactobacilli can produce different antimicrobial components including organic acids, hydrogen peroxide, low-molecular weight antimicrobial substances, bacteriocins and adhesion inhibitors and thus have gained prominence as probiotics.[24]

2.4. Recent trends in probiotics

2.4.1. Pathobiotechnology

The term "Patho-Biotechnology" was introduced by Sletor and Hill. It comprises of three basic approaches; Use of attenuated bacterial pathogens as vaccine, Isolation and purification of pathogen specific immunogenic protein for direct application, Equipping probiotics bacteria with genetic element necessary to overcome stress outside host, inside host and antagonize invading pathogens

2.4.2. Designer probiotics

This approach employs probiotics to be engineered to express receptor mimic structures on their surface, few studies done are limited to gut, periodontal studies are lacking, but poses a great potential in this field to develop. Designer probiotics have been employed in treatment of HIV, also employs as a novel vaccine delivery vehicle. Improving the stress tolerance profile of probiotic cultures significantly improves tolerance to processing stress and prolongs survival during subsequent storage. This in turn contributes to a significantly larger proportion of the administered probiotics that would reach the desired location (e.g., the gastrointestinal tract/periodontium) in a bioactive form.[25]

2.5. Risk associated with use of probiotics

2.5.1. Side effects and risks

Some live micro-organisms have a long history of use as probiotics without causing illness in people. Probiotics' safety has not been thoroughly studied scientifically. More information is especially needed on how safe they are for young children, elderly people, and people with compromised immune systems.

Side effects of probiotics, if they occur, tend to be mild and digestive (such as gas or bloating). More serious effects have been seen in some people. Probiotics might theoretically cause infections that need to be treated with antibiotics, especially in people with underlying health conditions. They could also cause unhealthy metabolic activities, too much stimulation of the immune system, or gene transfer (insertion of genetic material into a cell).[26]

Probiotic products taken by mouth as a dietary supplement are manufactured and regulated as foods, not drugs. Furthermore, uncertainty about specificity of probiotics effects and their mechanism of action is a cause of concern. Since probiotics contain live micro-organisms, there is a slight chance that these preparations might cause pathological infection, particularly in critically ill or severely immunocompromised patients.[27] Probiotic strains of Lactobacillus have also been reported to cause bacteremia in patients with short-bowel syndrome, possibly due to altered gut integrity.[28] Lactobacillus preparations are contraindicated in persons with a hypersensitivity to lactose or milk. S. boulardii is contraindicated in patients with a yeast allergy.[29]

3. Conclusion

Probiotics are emerging as a captivating field in periodontics. There is an increasing evidence that the use of existing probiotic strains can deliver periodontal health benefits. Further work will be needed to fully augment and compute the extent of this benefit. In parallel, the potential of prebiotics to maintain and enhance the benefits provided by the resident oral microbiota should be investigated. However, whether considering probiotics or prebiotics, it will be essential to develop an understanding of the broad ecological changes induced in the mouth by their ingestion and the long-term consequences of their use on oral health and disease. Further studies to understand the ability of probiotic bacteria to survive, grow, and have a therapeutic effect when used for treatment or when added to foods, to fix the doses and schedules of administration of probiotics should be undertaken. Hence, systematic studies and randomized controlled trials are needed to find out the best probiotic strains and means of their administration in different oral health conditions. Better scientific understanding and extended research of these tiny forms of life and their effect on humans in the treatment of various forms of periodontitis might further broaden the field of potential applications.

4. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

5. Source of Funding

None.

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