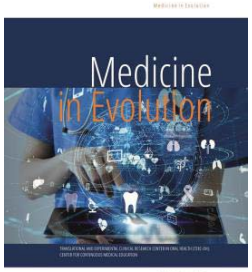
# Probiotic Therapy and the Oral Microbiome




**Sava-Rosianu R.[1], Galuscan A.[1], Jumanca D.[1], Oancea R.[1], Balean O.[1], Sfeatcu R.[2], Dumitrescu R.[1], Alexa V.[1], Bolchis V.[1], Buzatu B.[1], Floare L.[1], Muntean A.[3]**

[1]*Translational and Experimental Clinical Research Centre in Oral Health, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania*
[2]*University of Medicine and Pharmacy "Carol Davila" Bucharest*
[3]*Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania*

*Correspondence to:*
*Name: Balean Octavia*
*Address: Timisoara, Splaiul Tudor Vladimirescu nr. 14A*
*Phone: +40 748677191*
*E-mail address: balean.octavia@umft.ro*

*Received: 17 January 2024; Accepted: 29 February 2024; Published: 31 March 2024*

## Abstract

The aim of this randomized controlled trial is to obtain an enhancement of general oral health by supplementing the daily oral hygiene with a three-month oral probiotic therapy. For this randomized clinical trial, patients for the study group were selected meeting defined inclusion and exclusion criteria and Gingival Probing Deapth (GDP), Bleeding on Probing (BOP) and pH was measured before and after using probiotic therapy. For statistical analisys, the data was transferred from the periodontal chart into an Excel sheet. The results were presented by means of descriptive analysis, followed by the statistical analysis with the Fisher's exact test, testing whether the null-hypothesis is rejected. In the study group, nine out of ten patients showed an improvement after the treatment phase, and one patient did not present an improvement. In the control group seven out of ten patients showed an improvement, and three patients did not. The test resulted in $p = 0.291$, thus $p > 0,05$, which means, that there was no statistical significance in improvement in the two groups for GPD. Only those participants were included in the database, which demonstrated BOP > 0 during the first measurement. In the study group eight patients were included in the study, of which all presented an improvement in BOP after the oral probiotic therapy. In the control group four patients were included in the study, of which no patient presented an improvement. The test resulted in $p = 0.002$, thus $p < 0.05$. The improvement in the two groups for BOP was considered statistically very significant. In conclusion, improvements have been obtained by a decrease in BOP. Although the intake of oral probiotics on GPD and salivary pH did not show statistical significance, positive changes have also been noted. Further studies are needed to prove the beneficial effects of oral probiotics on oral health.

**Keywords:** probiotic therapy, oral health, oral pH, BOP

## INTRODUCTION

Probiotics are described as living, nonpathogenic bacteria that, when administered in the proper dosage, may have a favorable effect on the host organism (1). A rising interest regarding oral and systemic health is noted since dental health is a crucial factor in life quality. Thus, preventive treatment is considered as essential in oral health. The increasing demand for the prevention of oral diseases and the promotion of oral health, rather than just treating dental problems, causes the patients to be more inclined to obtain a higher standard of oral health promotion service. In the last couple of years, the introduction of probiotics in the field of dentistry has drawn attention and has shown promising affects in terms of oral health.

Probiotics are already widely utilized for general health, especially in gastroenterology. They aid in inhibiting pathogenic colonization and the spread of disease and furthermore stimulate flora that incites health. They reinforce the immune system to fight against allergies, stress, toxicants, and other diseases (2). They develop their health-promoting properties on the one hand through direct local inhibition of competing microorganisms and on the other hand through contact with cells of the mucosal immune system, which are found in all mucosal membranes.

Complex immunological regulatory mechanisms are initiated, that can influence the strength of inflammatory reactions, at the site of direct contact, and also systemically in other regions of the body. In addition, probiotics can stimulate mucosal cells to produce more antibacterial mucus and improve the tightness of the epithelial barrier against penetration of harmful substances and germs (3). Especially in the arising era of antibiotic resistance, the use of oral probiotics seems to facilitate new possibilities in the treatment and the prevention of diseases. The oral cavity is a microbiological medium that requires homeostasis.

The oral microbiome is made up of more than 700 different species (4). Apparently only 54% of them are yet identified with title and culture, 14% are cultured but not titled and the residual 32% are untitled. The oral cavity is characterized by a great diversity of microorganisms like bacteria, viruses, fungi, archaea and protozoa. The dominating microorganisms are bacteria.

Several niches in the oral cavity present different features like the soft tissue lining of the oral mucosa and tongue, the hard tissue lining of the teeth, and the saliva. Every niche has a distinct ecosystem, which provides an ideal environment and nourishment for the inhabiting microorganisms.

The balance between the host and the microbial species that coexist in it is crucial for oral health at all stages of life. However, it is quite difficult to maintain this equilibrium, and many factors might disturb it like general dietary behavior, sugar intake, cigarette smoking, dental hygiene, and utilization of antibiotics and other antimicrobials (5).

Factors like poor oral hygiene, nutrition, and immunosuppression can disturb the equilibrium, leading to oral infections. These might need extensive therapy due to their polymicrobial nature (1).

Currently, a variety of microorganisms are applied as probiotics. The most commonly used bacteria belong to the species Lactobacillus, which is the largest group of bacteria to be considered as probiotics, and the Bifidobacterium and Streptococcus (6,7). These bacteria are naturally inhabiting the system and do not present any adverse effects (7).

The Food and Drug Administration in the United States has declared the following probiotics to be generally considered safe: *Lactobacillus reuteri; Lactobacillus acidophilus*, *Lactobacillus lactis, Pediococcus acidilactici*; *Lactobacillus casei subsp. Rhamnosus*; *Bifidobacterium*

*longum*; *Bifidobacterium lactis* and *Streptococcus thermophilus*; *Carnobacterium maltaromaticum*; *S. cerevisae* and *Saccharomyces cerevisae* (8).

Their exact mechanism of action in the oral cavity is still unknown, but they are capable to disturb the imbalance existing in biofilm-associated infections.

In terms of oral hazards, probiotic bacteria may minimize the prevalence of infections linked to dental caries (mutans streptococci) (6). Systemic antimicrobial medications may be necessary for the treatment of these diseases, which can lead to gastrointestinal side effects because of broad spectrum antibiotics, bacterial resistance, and allergic reactions. This is why several authors have suggested alternate treatments that can provide significant benefits without doing harm to the patient.

Oral probiotics have displayed successful results in caries prophylaxis, reduction of oral candida counts, periodontal disease management, and in the treatment of halitosis. Lately, probiotic therapies have been established, that target the disruption of cariogenic bacteria. Studies have shown that probiotics are able to temporary decrease the amount of streptococci in saliva and plaque (6).

The presence of pathogenic bacteria and the absence of favourable bacteria can contribute to the onset of periodontal disease. Conventional therapy methods aim the reduction of pathogenic bacteria and include mechanical subgingival debridement, sometimes in combination with antibiotics, and oral hygiene enhancement. Currently, the application of probiotics to re-establish the right number of favourable bacteria in the oral cavity has attracted more attention.

Significant diversity in patient population and investigated variables make it difficult to analyze the existing data. For instance, different degrees of periodontal disease (gingivitis, chronic periodontitis and aggressive periodontitis) and several examined parameters, like measuring pocket depths, bleeding on probing, microbiologic factors in saliva and plaque, and various markers for gingivitis and plaque interfere with the analisys.

### *Aim and objectives*

In this study, the focus was set on the effect of the oral probiotic on Gingival Probing Depth (GPD), Bleeding On Probing (BOP), and on the salivary pH. The aim of this randomized controlled trial is to obtain an enhancement of general oral health by supplementing the daily oral hygiene with a three-month oral probiotic therapy. The applied oral probiotic is a pharmaceutical product, acquirable without prescription, and easy to include in the daily routine.

## MATERIAL AND METHODS

For this randomized clinical trial, patients for the study group were selected meeting defined inclusion and exclusion criteria. Compatible patients were found for the control group to achieve comparability between the two groups. Each group compromised 10 patients. The patients were requested to maintain their habitual oral health care during the 3 months trial-period. Inclusion and exclusion criteria were defined to achieve a uniform and appropiate study population

During the first appointment, the pH value of the saliva was measured with the indicator paper “Uralyt-U”. The patient was requested to not eat, drink, smoke or brush the teeth at least one hour before the measurement to not affect the results. The patient was instructed to collect saliva in a sterile tube and the indicator paper was immersed in the tube for two seconds. After 5 seconds, the color of the indicator paper was compared to the colour scale to determine the pH-value (9). The normal range of salivary pH ranges from 6.2-7.6 with

6.7 being the average value. Values above 7.6 indicate an alkaline environment and values below 6.2, an acid environment (10).

The measurement of gingival probing depth and bleeding on probing (BOP) was performed with a Williams periodontal probe, which is blunt-tipped and marked with a millimeter-scale. The gingival depth measurement is carried out by inserting the probe into the space between tooth and gingiva parallel to the root surface. Minimal pressure (0.25N) is applied until further insertion is inhibited by resistance as the probe tip reaches the bottom of the pocket. Probing depth assesses the width between the probe tip and the gingival margin.

Probing depth can vary depending on the site of the tooth, local anatomy, probing force, and angulation-, thickness-, and type the probe. Probing depth reproducibility and intra-clinician discrepancies were observed.

Subjects of the study group were instructed to take in the probiotics („OraLactin'', „BioLactis'', Cumdente, Germany) once daily after a meal for 3 months. It is a natural dental care cosmetic to support the oral immunity, to prevent caries and gingival diseases, and acts against halitosis. The oral probiotic contains gram positive bacterial strains, like lactobacilli and bifidobacteria, which can inhibit the growth of pathogenic bacteria or selectively kill them. Furthermore, probiotic bacteria produce oxygen derivates, which helps to reduce the pathogenic anaerobe bacteria. The powder gets a viscous consistency through the saliva and is rinsed in the oral cavity for 60 seconds.

After 3 months of probiotic therapy of the study group and no therapy of the control group, GPD, BOP and salivary pH were tested again and the results were transferred into a periodontal chart for the reevaluation.

For statistical analisys, the data was transferred from the periodontal chart into an Excel sheet. Per participant there were 146 data points collected for each of the two measurements: 144 gingival probing depths (if 32 teeth present, four probing values each; if missing tooth, respectively no probing value measured), one pH and one bleeding value. These data points were treated as dependent data points as they are the result of the binary independent variable that is if a treatment was undertaken.

The GPD variable in ratio scaled as the metric (measured in mm) has a true zero and equal intervals between neighboring points. For the purpose of the analysis, the mean GPD across all 144 (or less, if not all 32 teeth present) measurements was taken as the underlying question looked at an overall improvement of the oral health and not that of specific teeth.

PH is an interval scaled variable on a linear scale but not relative to a true zero (similar to temperature). In absence of a true zero, relative comparisons can be made but ratios and proportions are not meaningful. BOP is an absolute scaled variable as it counts the number of bleeding points when performing periodontal probing. Thus, its natural origin is zero with clear ordering.

For the purpose of this work, changes were templated into binary values, where a binary value of zero depicts no improvement, whereas a binary value of one depicts an improvement. An improvement has a different interpretation for GPD and BOP than for salivary pH. An improvement was defined as a decrease in value of GPD, and a decrease in the BOP is reflecting less bleeding.

The results were presented by means of descriptive analysis, followed by the statistical analysis with the Fisher's exact test, testing whether the null-hypothesis is rejected or not.

## RESULTS

Nine patients of the study group showed an improvement in GPD, denoted by the binary value "1". Only one patient did not showing an improvement, denoted by "0".

The mean decrease in gingival probing depth of the study group counted -5%.

In the control group, seven patients showed an improvement in GPD, and three patients did not present an improvement. The mean decrease in gingival probing depth of the control group counted -1%.

In the study group, eight patients showed a decrease in the number of BOP, which displays an improvement. In the control group none of the participants showed an improvement in BOP after the treatment.

Regarding pH values, one patient in the study group demonstrated an improvement in the salivary pH, denoted by the binary value 1. The salivary pH in the first measurement was 5.9, and at the second measurement 6.7. All other patients of the study group did not present an improvement in the salivary pH, denoted by the binary value "0". They presented a pH-value inside the normal range of salivary pH at the first measurement, and also displayed a pH-value inside the normal range at the second measurement. In the control group, no patient showed an improvement of the salivary pH. All patients of the control group presented a pH-value in the normal range at the first measurement, and at the second measurement as well. The study group had a mean pH of 6.58 at the initial measurement and 6.81 at the second measurement. The control group presented a mean pH of 6.63 at the initial measurement and 6.61 at the second measurement.

The counts of "improvements" and "no improvements" of GPD were transferred into the 2x2 contingency table (Fig. 1). In the study group, nine out of ten patients showed an improvement after the treatment phase, and one patient did not present an improvement. In the control group seven out of ten patients showed an improvement, and three patients did not. The test resulted in p = 0,2910, thus p > 0,05, which means, that there was no statistical significance in improvement in the two groups for GPD.

| | Improvement | No improvement | Total |
|---|---|---|---|
| Study | 9 | 1 | 10 |
| Control | 7 | 3 | 10 |
| Total | 16 | 4 | 20 |

**Fisher's exact test**

The one-tailed P value equals 0,2910

The association between rows (groups) and columns (outcomes) is considered to be not statistically significant.

Figure 1. Probing depth alterations between study group and control group

Only those participants were included in the database, which demonstrated BOP > 0 during the first measurement. In the study group eight patients were included in the study, of which all presented an improvement in BOP after the oral probiotic therapy. In the control group four patients were included in the study, of which no patient presented an improvement. The test resulted in p = 0.0020, thus p < 0.05. The improvement in the two groups for BOP was considered statistically very significant.

| | Improvement | No improvement | Total |
|---|---|---|---|
| Study | 8 | 0 | 8 |
| Control | 0 | 4 | 4 |
| Total | 8 | 4 | 12 |

**Fisher's exact test**

The one-tailed P value equals 0.0020

The association between rows (groups) and columns (outcomes) is considered to be very statistically significant.

Figure 2. Bleeding on probing – changes in the control and study group

In the study group, one out of ten patients presented an improvement in salivary pH after the oral probiotic treatment, and nine patient presented no improvement. In the control group zero out of ten patients presented an improvement in salivary pH, and ten patients demonstrated no improvement.

| | Improvement | No Improvement | Total |
|---|---|---|---|
| Study | 1 | 9 | 10 |
| Control | 0 | 10 | 10 |
| Total | 1 | 19 | 20 |

**Fisher's exact test**

The two-tailed P value equals 1.0000

The association between rows (groups) and columns (outcomes) is considered to be not statistically significant.

Figure 3. pH measurements within the control and study group

The test resulted in $p = 1.0000$, thus $p > 0.05$. The improvement of salivary pH in the two groups was considered not to be statistically significant.

## DISCUSSIONS

The experimental study was aimed to estimate the effect of the oral probiotic "OraLactin" ("BioLactis") on the oral health, tested on three parameters, GPD, BOP, and salivary pH. The results were obtained by two different approaches. As first instance, the data of the study group and control group was compared by descriptive analysis, which should give a more detailed overview about the obtained results of the two groups. Next, statistical analysis was performed with the Fisher's test to establish, whether the null hypothesis is rejected or not. The comparison of the results of the two groups concerning GPD showed that there was a greater improvement in the study group than in the control group. In the study group nine out of ten patients presented an improvement, and in the control group seven out of ten people improved their GPD.

The mean decrease of GPD in percentage enables a more precise evaluation. The study group presented a mean decrease of -5%, whereas the control group demonstrated a mean decrease of only -1%. Although in the control group a considerable number of participants

presented an improvement in GPD at the second measurement, the extent of improvement was by far not as great as the improvement in the study group.

The fact, that also in the control group an improvement in GPD was identified, even no oral probiotic was taken in might be explained by the Hawthorne effect. This effect supposes that patients may have carried out a more thorough and a more regular dental hygiene at home, due to their awareness of being monitored in the clinical study, even though they were asked to maintain their ordinary dental hygiene (11). In the study conducted by Krasse *et al*. one of two *L. reuteri* formulas was administered to participants with moderate to severe gingivitis, and it was stated that they had less plaque and gingivitis levels than the placebo group (12). Therefore, reason for the decrease in GPD could be the reduction of enlarged gingiva in areas of gingivitis.

A systematic review and meta-analysis of clinical trials about the supplementary use of probiotics to periodontal treatment, researched by Louis Hardan *et al*., demonstrated the gain of clinical attachment in periodontitis patients after SRP in conjunction with probiotics (13).

No evidence was found for clinical attachment gain only after oral probiotic therapy without SRP. In the clinical practice guideline conducted by Mariano Sanz *et al.* the use of probiotics as supplementation to subgingival instrumentation in periodontitis patients is discouraged. No statistical significance could be obtained in the mean difference in probing pocket depth between probiotics and placebo. Solely the probiotic formulation containing *L. reuteri* demonstrated improved probing depth reductions (14).

Opposing the results of BOP of both groups, eight patients of the study group presented an improvement, whereas in the control group no patient showed an improvement.

It is to mention, that for two patients of the study group, and for six patients of the control group no improvement was possible to achieve, because their initial BOP value was 0.

This significantly decreases the sample size, because only those patients with a BOP > 0 were included in the study, which considerably affects the meaningfulness of the study.

For future studies, it is be recommended to include only those patients in the study group and in the control group, which present a BOP > 0 at the first measurement.

Nevertheless, referring only to those patients included in the study with a BOP > 0 at the first measurement, all patients of the study group demonstrated an improvement in BOP, in contrast to the control group, where no patient presented an improvement. In the double-blind, placebo-controlled randomized controlled trial conducted by Mi-Sun Kang *et al.* an improvement in the bleeding index was recognized in the study group taking in oral probiotic tablets for 8 weeks after SRP (15). Bleeding on probing is a key indicator used to determine gingivitis. The insertion of a periodontal probe causes bleeding, if the gingiva is inflamed and the pocket epithelium is atrophic or ulcerated, which is thought to be mediated by subgingival pathogenic bacteria (13).

For the Fisher's exact test as well, only those patients with a BOP > 0 at the first measurement were included. The test resulted in $p = 0.0020$, thus $p < 0.05$. The improvement in the two groups for BOP was considered statistically very significant.

Disregarding the small sample size, the oral probiotic therapy seems to have a positive impact on gingival bleeding on probing. The systematic review and meta-analysis by Zohre Gheisary *et al*., published in 2022, advocates the outcome of the study. Included in the studies were patients with or without periodontal disease, but most of them focused on patients with periodontal disease. In the study groups, different forms of probiotics were taken in for a deviating treatment duration from one day to four months, and the sample sizes variegated from 10 to 120 patients. The control groups did not receive any probiotic treatment. The effect of probiotics on BOP in patients with periodontal disease showed a statistically significant decrease in the study groups, in comparison to the control groups (16).

In this study, only those patients were considered to have obtained an improvement, who presented a salivary pH outside the normal range at the initial measurement, and inside the normal range at the second measurement. One patient of the study group presented an improvement, by an increase of salivary pH from 5.9 to 6.7. According to research, the determining factor for the onset and advancement of caries is pH rather than sugar. Low salivary pH encourages the growth of acidic bacteria, allowing these to multiply and thereby causing an unfavourable environment for the defending oral bacteria. This enables a change in the environment that favours cariogenic bacteria and further lowers the pH of the saliva. By regulating pH, it is possible to modify plaque biofilms, remineralize lesions, and possibly even prohibit the disease (17). The other nine patients demonstrated a pH value inside the normal range at the initial measurement and at the second measurement as well. In the control group no patient displayed an initial pH-value outside the normal range.

To mention also those changes, which have taken place inside the interval of the normal salivary pH, the mean pH-values at the first and second measurements were compared between the study and control groups. The study group showed an increase of the salivary pH of 0.23 after the oral probiotic treatment (6.58 - 6.81). In the control group the pH changed with 0.02 (6.63 - 6.61).

A study conducted by Shashibhushan Kukkalli Kamalaksharappa *et al.* evaluated the efficacy of probiotic and green tea mouthrinse on salivary pH in children and the comparison of pre- and post-mean pH of the probiotic group showed an increase of pH from 6.45 - 6.65 towards the mean salivary pH value. Anyhow the results did no show statistical significance (17). The improvement of the salivary pH in the two groups was considered not to be statistically significant ($p > 0.05$).

In the present study no standardization of the oral hygiene status of the participants was performed by oral prophylaxis prior to the trial. This might have led to potential distortions of the study outcomes and it is advisable to do in order to create as similar preconditions as possible.

Another limitation is referring to GPD. The statistical test did not show any significance in improvement in the two groups for GPD. The data included in the Fisher's exact test might not be compelling enough, because any decrease in GPD was considered to be an improvement no matter the size (< 0). A delimitation of the size of the decrease of GPD considered an improvement would be useful by taking into account only more significant decreases in probing depth, for example < -5 %. This would exclude a significant number of participants, which were now in this study considered to present an improvement in GPD.

A further limitation pertaining to GPD is the inclusion of the general population in the study, without distinguishing between health, gingivitis and periodontitis. In fact, testing the effect of the oral probiotic on the general population was the intention of the study, but it makes the interpretation of the results fairly difficult. Furthermore, the small sample size states a drawback. This refers especially to the evaluation of the bleeding index, where not all participants were suitable for the trial, because of their initial bleeding index of zero. No further improvement could be obtained so the concerned participants were excluded from the study sample. Thus, especially those results should be interpreted with caution.

In this study, mainly clinical parameters have been tested. To obtain further explanations for the effect of oral probiotics on the measured variables, the inclusion of microbiological or immunological parameters could be additionally implemented in the investigation. (12)

## CONCLUSIONS

In conclusion, improvements have been obtained by a decrease in BOP. The decrease in BOP indicates a reduction of pathogenic bacteria inducing inflammation of the gingiva. The link between BOP and microbiological parameters could be additionally investigated in future research. Although the intake of oral probiotics on GPD and salivary pH did not show statistical significance, positive changes have also been noted. Further studies are needed to prove the beneficial effects of oral probiotics on oral health.

## REFERENCES


1. Seminario-Amez M, Lopez-Lopez J, Estrugo-Devesa A, et al. Probiotics and oral health: A systematic review. Med Oral Patol Oral Cirugia Bucal. 2017;0–0.
2. Alok A, Singh I, Singh S, et. al. Probiotics: A New Era of Biotherapy. Adv Biomed Res. 2017;6(1):31.
3. Y Jockel-Schneider, Stötzel P, Schlagenhauf U. Entzündungsmodulation in der Parodontitistherapie: Pillen, Statine & Co. 2022. 2022 Nov 16;(04).
4. Yamashita Y, Takeshita T. The oral microbiome and human health. J Oral Sci. 2017; 59(2):201–6.
5. Santonocito S, Giudice A, Polizzi A, et al. A Cross-Talk between Diet and the Oral Microbiome: Balance of Nutrition on Inflammation and Immune System's Response during Periodontitis. Nutrients. 2022 Jun 11;14(12):2426.
6. Laleman I. Probiotics in the dental practice: A review. Quintessence Int. 2015 Jan 23;46(3):255–64.
7. Thantsha MS, Mamvura CI, Booyens J. Probiotics - What They Are, Their Benefits and Challenges. In: Brzozowski T, editor. New Advances in the Basic and Clinical Gastroenterology [Internet]. InTech; 2012 [cited 2022 Jul 31]. Available from: http://www.intechopen.com/books/new-advances-in-the-basic-and-clinicalgastroenterology/probiotics-what-they-are-their-benefits-and-challenges-
8. Chalas R, Janczarek M, Bachanek T, et al. Characteristics of oral probiotics – a review. Curr Issues Pharm Med Sci. 2016 Apr 1;29(1):8–10.
9. Said O, Razumova S, Velichko E, et al. Evaluation of the Changes of Salivary pH among Dental Students Depending on Their Anxiety Level. Eur J Dent. 2020 Oct;14(04):605–12.
10. Baliga S, Muglikar S, Kale R. Salivary pH: A diagnostic biomarker. J Indian Soc Periodontol. 2013;17(4):461.
11. Shafqat S, Akram Z, Aati S, et al. Clinical efficacy of probiotics in the treatment of gingivitis: A systematic review and meta-analysis. 2019.
12. Gupta G. Probiotics and periodontal health. J Med Life. 2011 Nov 14;4(4):387–94.
13. Hardan L, Bourgi R, Cuevas-Suárez CE, et al. The Use of Probiotics as Adjuvant Therapy of Periodontal Treatment: A Systematic Review and Meta-Analysis of Clinical Trials. Pharmaceutics. 2022 May 9;14(5):1017.
14. Sanz M, Herrera D, Chapple I, et al. Treatment of stage I–III periodontitis—The EFP S3 level clinical practice guideline. J Clin Periodontol. 2020 Jul;47(S22):4–60.
15. Kang MS, Lee DS, Lee SA, et al. Effects of probiotic bacterium Weissella cibaria CMU on periodontal health and microbiota: a randomised, double-blind, placebo-controlled trial. BMC Oral Health. 2020 Dec;20(1):243.
16. Gheisary Z, Mahmood R, Harri Shivanantham A, et al. The Clinical, Microbiological, and Immunological Effects of Probiotic Supplementation on Prevention and Treatment of Periodontal Diseases: A Systematic Review and Meta-Analysis. Nutrients. 2022 Feb 28;14(5):1036.
17. Kamalaksharappa S, Rai R, Babaji P, et al. Efficacy of probiotic and green tea mouthrinse on salivary pH. J Indian Soc Pedod Prev Dent. 2018;36(3):279