PROBIOTICS AND ORAL HEALTH: A REVIEW

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ABSTRACT

Probiotics are non-pathogenic living microbes used to treat several medical conditions. They have been added in a few food products due to their favourable results on human health. The mechanism of action of probiotics is associated with their capacity to cope with pathogenic microorganisms for adhesion sites, to antagonize these pathogens or to regulate the host's immune response. Probiotics might be helpful in intercepting and treating oral infections, including dental caries, periodontal disease and halitosis. Probiotics contribute to a healthy microbial balance by interacting with oral micro biome which impacts the general health, being a significant contributor to oral health. The development of drug resistance and the side effects of available antimicrobials have confined their use in an array of prophylactic options. Currently, no such evidence exists to support the use of probiotics to prevent, treat or manage oral cavity diseases. Probiotics don't have any adverse effects and there is no evidence of being used for the treatment or as a preventive measure for the oral health. In this review, author tried to explore the use of probiotics in prevention, treatment and management of oral cavity diseases and the possibilities of developing designer probiotics for the next generation of oral healthcare.

Keywords: Probiotics; Lactobacillus; Dental healthcare; Periodontics.

INTRODUCTION

The oral cavity is made up of 700 bacterial species or phylotypes, of which over 50% have not been cultivated. (1)The dietary benefit of microorganism has a long history. Farm products like kefir, koumiss, liben and curd, were frequently used before the existence of microorganism was acknowledged. Facts concerning the significance of farm products is found in the bible and the Bhagavad Gita. (8) For over a number of years, few probiotic bacterium have been added to food products because of their valuable addition to the health of the living beings. (2) The optimistic outcomes of probiotics in general health have resulted in their outspread. Primary use of probiotics

focuses on managing the intestinal tract problems. (4) The word probiotics originates from a Greek word meaning "for life." The Food and Agricultural Organisation of the United Nations (FAO)/WHO in 2001 defined probiotics as "live microorganisms, when administered in adequate amounts; confer a health benefit to the host." (5), (6), (7) Probiotics are a positive influence on animals and human health. In 1994, the World Health Organisation (WHO) stated probiotics as the upcoming most important immune defense system when regularly prescribed antibiotics are rendered meaningless. (3) Use of lactic acid bacilli in health through regular ingestion was proposed by Ukrainian bacteriologist Ilya Metchnikoff in 1908. In 1950, a probiotic product was rubbed on pigs' skins for cleaning purpose. (2) In 1965, Lilley and Stillwell established the word probiotics as an opposite to antibiotics. In 1974, Mann and Spoering noticed the reduction of blood serum cholesterol levels by use of fermented yogurt. (8) Hull in 1984 discovered the first probiotic species, the *Lactobacillus acidophilus*. (8) Numerous clinical researches have proven their usefulness in treating cancer and dental caries. (8) The purpose of diet in health and well-being is universally acknowledged. Progress in nutritional science has intended towards apprehending the physiological effects of diet apart from the nutritional effect. Probiotics are the subject of a widespread research in food and nutritional science including oral health.

Probiotics are provided in products in one of the following basic ways:

- 1) A culture concentrate which is added to a beverage or food, for example, fruit juices.
- 2) Infused into prebiotic fibres.
- 3) Added into a milk-based food, for example, dairy products such as milk, milk shakes, yogurt, cheese, kefir, and bio drink sauerkraut, kvass, natto, kombucha. [Figure 1]
- 4) As concentrated and dried cells packaged as dietary supplements (non-dairy products) such as powder, capsule, and gelatin tablets. (10), (11)

Figure 1: Ideal Properties of a probiotic intended for use in disorders of the mouth

COMPOSITION OF PROBIOTICS:

Probiotics can be yeast, bacteria or moulds. Most commonly they are bacteria. Some of these bacterial species are:

- Lactic acid producing bacteria (LAB): Lactobacillus, Bifidobacterium, Streptococcus.
- Non Lactic acid producing bacteria (LAB) species: Bacillus, Propionibacterium
- Non-pathogenic yeasts: Saccharomyces
- Non spore forming and non-flagellated rod or Coccobacilli⁽¹²⁾

CHARACTERISTICS OF PROBIOTICS:

Probiotics are living microorganisms, safe for consumption, which have a beneficial effect in health. A fully characterized bacterial strain can be called a probiotic. The FAO and the WHO have advised that probiotic bacterial strains should be distinguished by their ability of resistance to antibiotics and haemolytic activities, their capacity to produce toxins, their infectious power in immuno compromised animal models and their side effects in human beings. These probiotics strains should be submitted to randomized clinical trials. The outcome of such studies should indicate betterment of health. (2)

MECHANISM OF ACTION OF PROBIOTICS:

Mechanisms to be explained how probiotics are (Fig. 1). For example, these bacteria secrete different antimicrobial substances like organic acids, hydrogen peroxide and bacteriocins.⁽⁷⁰⁾ In addition, they compete with pathogenic agents for adhesive sites on the mucosa.^{(68) (71)} Probiotics can change the surrounding environment by regulating the pH and/or the oxidation–reduction

potential, which may compromise the ability of pathogens to become established. Finally, probiotics may yield valuable results by stimulating nonspecific immunity and regulating the humoral and cellular immune response.⁽⁷²⁾ A combination of probiotics is often used to increase beneficial effects.⁽⁶⁹⁾

CHARACTERISTICS OF CLASSIC PROBIOTIC MICROORGANISMS

- 1) Must restore and endure the intestinal micro flora.
- 2) Must adhere to the intestinal mucosa or the target tissue.
- 3) Must be ready to survive and metabolize in the gut environment, for example: Defiance to low pH.
- 4) Should have useful result on host animal.
- 5) Must be viable under storage for longer duration.
- 6) Should be safe for human consumption and beneficial physiological effects should be scientifically demonstrable
- 7) Must be non-pathogenic and non- toxic.
- 8) Should be stable in acidic and alkaline environments.
- 9) Must be bacteriologically distinguished and shall have put.

PROBIOTICS AND PERIODONTOL DISEASES:

Periodontal diseases are- Gingivitis and Periodontitis

Gingivitis is defined as inflammation bounded to the unconnected gingiva, while periodontitis is a developing cataclysmic infection that attacks all the supportive tissues of the teeth as well as the alveolar bone. The primary microorganisms related with periodontitis are Porphyromonasgingivalis, Treponemadenticola, Tannerella forsythia, and Aggregatibacteractinomycetemcomitans.^{(17), (18)} The chief constituents for the forming of periodontal diseases are bacteria in supra and sub-gingival biofilms. Mucosal immune outcomes may be summoned by prebiotic booster dose. Their projected mechanism is building up a mucosal barrier via topical effects on the epithelium, and stimulation of both the innate and adaptive immune systems. A decrement in gum bleeding and faded gingival infection is been determined by Krasse et al. with the consumption of L reuteri, (19) Caglar E et al used L. reuteri containing bubble gums in 42 robust patients and evaluated the repercussions on the crevicular fluid volume(interleukin-1 β , interleukin-6, interleukin-10, and tumour necrosis factor-alpha [TNF- α]), cytokine levels and bleeding on probing.He found crevicular fluid volume, the levels of TNF- α and interleukin-8 and bleeding were all remarkably decreased.(17) As stated by KollKlais et al. probiotics consisting of Lactobacillus effected an 82% and 65%suppression in the development of P. gingivalis and Prevotellaintermedia.Riccia et al. utilized lozenges into whichL. brevis was integrated to study its anti-inflammatory effects in a set of patients having chronic periodontitis.

The report demonstrated momentous refinement, in plaque index, gingival index, bleeding on probing and remarkable reduction of inflamed gingiva. (20) Probiotic stains enclosed in periodontal dressings in ideal concentration of 108 CFU/mL have been shown

to lessen the number of constant stray periodontal pathogens: *Bacteroides* spp., *Actinomyces* spp., and *S. intermedius* and also *Candida albicans*.⁽²²⁾ Probiotic microorganisms might favour periodontal health and might also colonize a gingival pocket after scaling and root planing provided they are capable of launching themselves in the oral micro flora. Nevertheless additional longitudinal studies are needed to support these findings.

PROBIOTICS AND DENTAL CARIES:

Dental caries is a multi-step disease of bacterial derivation that is defined by acid demineralization of the tooth enamel. (23-25) *Streptococcus mutans* is a chief activating microorganism for caries. Raised amount of streptococcus counts are connected with increased escalated fear of dental caries. (24-26) To eliminate cariogenic bacteria present on the teeth surface to sustain against dental caries, firstly a probiotic microorganism should match the dental surface and combine into the bacterial community creating biofilms. Secondly, they should become a constituent of the biofilm which forms on the tooth surfaces and finally they should compete with cariogenic bacteria. All of this assists to reduce the cariogenic bacterial growth levels. (24-27) Nikawa et al. reported that intake of yogurt containing *Lactobacillus reuteri* over a period of 15 days dilutes *S. mutans* in the saliva by 80%. Proportionate outcomes were acquired by integrating probiotics in bubble gums or lozenges.⁽²⁵⁾ Probiotics incorporated in milk products neutralize acidity. For example, it has been observed that cheese forbids demineralization of the enamel and promotes its remineralisation.^(28, 29) In survey like Nse L and Meurman JH, single strain of *Lactobacillus rhamnosus* and the species *Lactobacillus casei* prohibited in vitro maturation of both the cariogenic streptococci, i.e. *S. mutans*, and *S. sobrinus*.^{(30), (31)} Lately, Petti et al. observed that yogurt consisting of *Streptococcus thermophilus* and *Lactobacillus bulgaricus* have selective bactericidal effects on streptococci of the mutans group. Lately clinical studies have exhibited the day-to-day consumption of yogurt, milk, or cheese consisting probiotics led to a drop-off in the amount of cariogenic streptococci in the saliva and a diminution in dental plaque.^{(17), (25), (29), (32), (33)} In 2001, Nse et al. published the survey of an 1.5 years of study of 594 children of 1-6 years which demonstrated their effects on dental caries of consumption of milk along with a strain of *L. rhamnosus*. They reached a conclusion that children who drink milk consist of this probiotic especially those who are 3-4 years old, had fewer dental caries and lower salivary counts of *S.*

PROBIOTICS IN ORAL HALITOSIS:

Oral malodor is a state which may impede the social life and self-esteem of an individual. Extensive approval for probiotic interference providing health benefits for non-intestinal body sites, application of it on alternative target tissues has increased, to obtain more specific and enduring benefits. Different studies have revealed the role of probiotic which help to decrease

inflammation of gingiva. Nevertheless, the survey of a stronger proof regarding the role of probiotics in treating and preventing oral malodor is less.⁽³⁴⁾

PROBIOTICS AND CANDIDIASIS:

Candida albicans amongst all is the most frequent infectious agent present in the oral flora. Eating probiotic cheese consisting *L. rhamnosus* GG and *Propionibacterium freudenreichii* ssp. *Shermanii* JS has shown a decrease in *C. albicans* count.⁽⁶⁴⁾

DISCUSSION:

Several mechanism have been proposed to justify how probiotics works. For instance, these bacteria stimulate numerous antimicrobial substances such as organic acids hydrogen peroxide, and bacteriocins.⁽³⁵⁾ Also their challenge is with pathogens for adhesive sites on the mucosa. In addition, probiotics also alter the surrounding environment by regulating the pH and/or the oxidation-reduction prospect which might square off the capability of pathogens to become habituated. In the end, probiotics might provide advantageous effects by stimulating nonspecific immunity and regulating the humoral and cellular immune response. An association of probiotic strains is frequently used to gain these advantageous effects.⁽³⁶⁾ The utilization of probiotics by human beings is almost entirely concentrated on obtaining the effects through the consumption of microorganisms primitively derived from intestinal sources.⁽³⁷⁾ The bacteria in milk and milk products comprises of the most important sources of probiotics for humans. (38) Most of the probiotic bacteria are a part of genera *Lactobacillus*, *Bifidobacterium*, *Propionibacterium*, and *Streptococcus*.^{(39), (40), (41)}

Various studies have shown the effectivity of certain probiotics in treating systemic and infectious diseases. Probiotics are largely used for "healthy gut." Nonetheless, the notion of alternative target sites has emerged.⁽⁴²⁾ Bernaola Aponte et al. in a survey inferred that there were limited grounds saying that probiotics can be beneficial in treating persistent diarrhoea in children.⁽⁴³⁾ Goldenberg et al. in a review declared that probiotic was both secure and efficient for avoiding clostridium difficile-associated diarrhoea.⁽⁴⁵⁾ Hao et al. discovered in their study on probiotics which aimed to prevent acute upper respiratory tract infection (URTI) that probiotics were found to be better than placebo in decreasing the number of candidates experiencing episodes of acute URTI by about 47% and the time span of an episode of acute URTI by about 1.89 days and might slightly decrease the antibiotic use, also side effects of probiotics were minor and gastro intestinal symptoms were the most common.⁽⁴⁶⁾ Then the concept of application of probiotic therapy in oral health was introduced. Apart from the use of probiotics in treating and preventing gastrointestinal tract infections, there have been studies performed to test the efficacy in the treatment and prevention of dental caries and periodontal diseases.^{(46), (47)} Yanine et al. in their review declared that the benefit of probiotics on the prevention and treatment of periodontal diseases is debatable.⁽⁴⁸⁾ The oral micro-flora is dwelling with a variety of bacterial species that produce numerous fetid substances as a result of protein degradation VSC

(volatile sulphur compound)-producing bacteria colonizing the dorsum of the tongue have recently been implied in oral malodour. Detection of VSCs, like methylmercaptan and hydrogen sulfite, through organoleptic and objective methods, can assist in the identification of their source. Following comprehensive evaluation for possible causes, most halitosis in patients seen in an ear, nose, and throat or dental practice can be localized to the tongue. ^{(49), (50)} Bacteriologic analysis of biofilm and scraped specimens obtained from the lingual dorsum and other oralsites, primarily gingival pockets and tonsillar crypts can identify VSC producing bacteria. *Porphyromonas*, *Prevotella*, *Actinobacillus*, and *Fusobacterium* species are the most common identified organisms. ⁽⁵¹⁾ Halitosis arising from the lingual dorsum secondary to overpopulated VSC-producing bacteria can be properly managed with a collection of mechanical cleansing using tongue brushes or scrapes and chemical solutions containing essential oils, zinc chloride, and cetylpyridinium chloride. ^{(52), (53), (54)} Using of mouthwash and doing dental treatments gives a short-term relief. Antimicrobial treatment randomly use up populations of both the problematic bacteria and those bacteria that are not thought to be implied in halitosis, but which might be essential in maintaining the normal oral micro-flora. The consequence of antimicrobial treatment is necessarily only a short-term decrease in malodour, until the halitosis-causing bacteria become re-established. Hence, probiotic therapy was used for treating halitosis ⁽⁵⁵⁾ Few problems occurred while performing the analysis, first, the types of pro-biotic studied varied throughout the trials, second and the most important issue, the variables were not reported decently in some of the surveys. Information on the outcomes of interest was only found in graphs and tables which did not allow acquiring the exact value of the final measurement in each group. ^{(58), (59), (61), (62), (63)}

Only 11 studies contributing to the results and conclusions are a very small number when compared to a large number of population affected due to oral malodour. All the surveys are of shortened time-span varying from 1-98 days. Therefore, do not shed light over the prevention aspect of probiotics over halitosis. It still lacks the evidence even though some studies have showed remarkable reduction in the halitosis levels as in two pilot studies which have decided that there was a remarkable reduction in the organoleptic scores and in production of the VSCs. A randomized clinical trial used commercially available probiotic drink, Yakult, as a vehicle of administration of probiotic, revealed no broad ecologic changes in the mouth and no noticeable effects on the halitosis levels, thus concludes that simply oral ingestion of probiotic has no effect on halitosis. ^{(56), (57)} Given the large number of internet sites devoted to the sale of probiotic products to people with oral malodour, one would expect that there are many well supported scientific claims of the effectiveness of these products. In reality, there are only countable few trials performed to assess the effectiveness of probiotics in the treatment of halitosis. There are various studies which have made use of probiotics in adjunct with other oral prophylactic products, but exclusive use of probiotics is scarce. In spite the limitations, we believe that this is the best possible summary of evidence of the topic. We advised conducting trials with appropriate sample sizes to have enough power to detect the differences among the groups and further

extensive studies to find out the potential of the probiotics in the prevention of malodour. ⁽⁶⁰⁾

SAFETY MEASURES:

Due to enhanced probiotics supplementation of different food products, safety measures are a leading concern. Probiotics are frequently regulated as dietary supplements instead of pharmaceutical or biological products. As a safety measure, probiotic microorganisms should not be pathogenic, should not have any maturation stimulating effects on bacteria causing diarrhoea, should not have an ability to transfer antibiotic resistance genes, and should not cause sepsis or bacteraemia. The probiotic should hold genetic stability in oral micro flora. Several events from antibiotic susceptibility tests claim that the tet- (W) and tet- (S) genes in some probiotic *Lactobacilli* and *Bifidobacterium* strains are accountable for sulfamethoxazole, gentamycin, polymyxin B and tetracycline resistance. These collection show the need of minimal safety rating during the selection of strains for probiotic use. ^{(65), (66)}

FUTURE APPLICATION:

Various applications of probiotics in general health can gain its demand. In future, probiotics can be used to cure many health issues. The important steps in many applications will be to make products available that are safer and clinically evidenced in a particular formulation, which should be easily available to physician and consumers. In India, *Sporolac* i.e., *Sporolacto bacilli* is a normally used probiotic. Lately, *Bacillus mesentericus* is used as an alternative to B-complex. ⁽⁶⁷⁾ Genetically enhanced lactic acid bacteria has been proposed as a vehicle to deliver vaccines in the gastrointestinal tract. ⁽⁶⁴⁾ Nanotechnology of probiotics is an area of emerging interest and opens up whole new possibilities for the probiotics use. Their applications to the agriculture and food sector are comparatively new compared with their use in drug delivery and pharmaceuticals. The basic of probiotic nanotechnology applications is presently in the development of nano-encapsulated probiotics. The nano structured food ingredients are being formed with the claims that they offer better taste, texture and consistency. Applications of nanotechnology in organic food production require safeguard, as little is known about their impact on environment and human health. In few recent food applications of nanotechnology, safety and risk problems of nano materials, routes for nano particles entering the body, existing regulations of nanotechnology in various countries, and lack of authorization system of nano products were reported ^(73, 74).

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