Review Article

PROBIOTICS-A LEGACY OF GOOD HEALTH

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ABSTRACT

Probiotics-means live microorganisms, which when administered in adequate amounts, confer a health benefit on the host. Probiotics can be bacteria, moulds, yeast. But most Probiotics are bacteria mainly lactic acid bacteria. The Probiotics have a three step action mechanism i. Stimulates and modulates immune response ii. Normalize intestinal micro flora iii. And also have the metabolic effects like. Probiotics have been analyzed for treatment and prevention of various diseases and disorders of human body and the results obtained are very encouraging. Probiotics have turned out to be very promising in ensuring oral health and general well being.

Key words: Probiotics, Oral Health, Immunity

INTRODUCTION

The term Probiotic was originally proposed in 1965 by Lilley and Stillwell to describe “substances secreted by one microorganism which stimulates the growth of another” and thus was contrasted with the term antibiotic. The human gastrointestinal micro flora, at present referred to as “microbiota” is a complex ecosystem of approximately 300–500 bacterial species comprising nearly two million genes (the so called “microbiome”). Gut microbiota is one of the most important key factors in maintaining and preserving the health of the entire body and has a reservoir of microorganisms naturally inhabiting the intestine as symbiotic. In lieu of the shelter that the human body provides, the intestinal flora performs several important functions in the human body such as fermenting undigested energy substrate, strengthening the immune system, protection against the growth of the pathogenic bacteria, promoting gut development, production of vitamins (such as Vitamin K and Biotin) and production of hormones for fat storage [1]. The idea of Probiotics was introduced in 1907, when , the Ukrainian born biologist and Nobel laureate Elie Metchnikoff realized that the consumption of Bulgarian Yoghurt (which contains lactic acid bacteria) was good for health. Probiotics have evolved for more than 10 decade back to present day [2].

Terminologies

Probiotics-means live microorganisms, which when administered in adequate amounts, confer a health benefit on the host (Guarner et al 2005).

Dysbiosis-occurs when there is an alteration in the normal balance of the micro-flora or organisms of the GIT. Dysbiosis can be controlled by simply fortifying the GI tract with ‘good bacteria’, known as Probiotics [3].

Prebiotics-are non digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already established in the colon, and thus in effect improve host health [4].

Synbiotic- is a product that contains both Probiotics and Prebiotics [5].

Replacement therapy-Also called ‘bacteriotherapy’ or ‘bacterial interference’ is sometimes used interchangeably with ‘Probiotics’. These include, the effector strain, which is not ingested but is applied directly on the site of infection. Also, colonization of the site by the effector strain is essential [6].

COMPOSITION OF PROBIOTICS

Probiotics can be bacteria, moulds, yeast. But most Probiotics are bacteria mainly lactic acid bacteria. Fuller in 1989 [7]. Listed the following organisms as species used in probiotic preparation: Lactobacillus bulgaricus, Lactobacillus plantarum, Streptococcus thermophillus, Enterococcus faecium, Enterococcus faecalis, Bifidobacterium species, and Escherichia coli. With the exception of L. bulgaricus and S. thermophillus, all the other organisms are all intestinal strains. A probiotic may be made out of a single bacterial strain or it may be a consortium as well (may contain any number up to eight strains). The advantage of multiple strain preparations is that they are active against a wide range of conditions and in a

wider range of animal species. Probiotics can be in powder form, liquid form, gel, paste, granules or available in the form of capsules, sachets, etc.

POTENTIAL MECHANISMS OF PROBIOTIC

The Probiotics have a three step action mechanism
i. Stimulates and modulates immune response,
ii. Normalize intestinal micro flora
a) Ensures colonization resistance
b) Controls irritable bowel syndrome and other inflammatory bowel diseases.
iii. And also have the metabolic effects like
a) Bile salt deconjugation and secretion,
b) Lactose hydrolysis,
c) Reduction in toxigenic and mutagenic reactions in gut.
d) Supply of nutrients to colon epithelium.

The mechanisms of probiotic action in the oral cavity could be analogous to those described for the intestine. Possible ways that Probiotics might affect oral health are summarized as follows.

Probiotics improve colonization resistance to gut pathogens by reinforcing the mucosal barrier and restoring normal gut micro ecology. They compete with pathogens for available substrate and direct antagonism through the production of bacteriocins or other products such as acids or peroxides. They protect epithelium barrier by maintaining tight junction protein expression and prevent apoptosis of mucous membrane, reduces inflammation by increasing production of anti-inflammatory cytokines and reducing the production of pro-inflammatory cytokines, stimulate dentritic cells resulting in expression of Th1 or Th2 responses, which modulate immunity, and compete with pathogens for binding site. Aggregation alteration is another mechanism of action. Probiotics stimulate apoptosis of tumor cells through end product formation and improve intestinal barrier integrity and up regulate the mucin production [8].

CRITERIA OF AN IDEAL MICROORGANISM USED AS PROBIOTICS

Ideal probiotic should have high cell viability, resistant to low ph and acids. It should have the ability to persist and adhesion to cancel the flushing effect, able to interact or to send signals to immune cells. It should be of human origin, non pathogenic, resistance to processing, must have capacity to influence local metabolic activity.

Probiotics bacteria seen in commercial preparations are Lactobacillus acidophilus which many either has no active species or had other species. Another important concern is dose of Probiotics required for adequate action, seen with differing values, of $1\times10^{8-10}$, $1\times10^{9-10}$, $1\times10^{10-11}$ [9].

PROBIOTICS IN GENERAL USE [10].

Proven indication

1. Rota virus diarrhoea
2. Reduction of antibiotic associated side effect

Possible indication

1. Dental caries and periodontal health
2. Food allergies and lactose intolerance
3. Atopic eczema
4. Prevention of vaginitis
5. Urogenital infections
6. Irritable bowel disease
7. Cystic fibrosis
8. Traveler's diarrhoea
9. Enhance oral vaccine administration
10. Helicobacter pylori infection
11. Various cancers

DESIGNER PROBIOTICS

The term "Patho-Biotechnology" was introduced by Sletor and Hill. It comprises of three basic approaches.

a. Use of attenuated bacterial pathogens as vaccine.
b. Isolation and purification of pathogen specific immunogenic protein for direct application.
c. Equipping Probiotics bacteria with genetic element necessary to overcome stress outside host, inside host and antagonize invading pathogens is termed as "designer Probiotics".

This approach employs Probiotics to be engineered to express receptor mimic structures on their surface. 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 would reach the desired location (e.g., the gastrointestinal tract or Periodontium) in a bioactive form [11].

PROBIOTICS: VARIOUS PERSPECTIVES

PROBIOTICS AND ORAL HEALTH

Evidences are there which proves that oral cavity is a natural habitat for some probiotic species. Hojo et al

[12] have found that Lactobacillus salivarius, Lactobacillus gasseri, Lactobacillus fermentum and Bifidobacterium are among the most prevalent species in the mouth in oral health status. Studies have shown that, to be able to exert Probiotic properties in the oral cavity it is essential for the micro-organisms to resist the oral environmental conditions and defense mechanisms, to adhere to the saliva coated surfaces, to colonize and grow in the mouth, to inhibit oral pathogens and to be also safe for the host [13]. Probiotic therapy decreases the risk of colonization by oral pathogens without depleting the friendly microflora. The inability of the antibiotics to discriminate good bacteria from the disease causing bacteria, the development of antimicrobial resistant mutants and the increasing rate of antibiotic associated side effects and complications suggests an urgent need to switch our therapeutic approach from traditional antibiotics to the probiotic therapy for oral care [14].

A particular concern when evaluating Probiotic effects on oral health relates to the means of administration of these bacteria. Generally Probiotics are delivered in dairy products (mainly fermented milks), as food supplements in tablet forms or in soft drinks. However these routes of administration cannot provide prolonged contact with oral tissues, facilitating Probiotic adhesion to saliva coated surfaces. A lozenge form or chewing gum tablet or gum might better serve the needs for periodontal health prophylaxis [15].

PROBIOTICS AND HALITOSIS

Oral halitosis refers to bad breath originating from the oral cavity. It regularly affects about one in four adults and frequently is caused by bacteria residing on the dorsal surface of the tongue, teeth which produce volatile sulphur compounds (VSCs) [16]. Increased VSC levels also may play a role in the link between oral infection and systemic diseases such as heart disease and preterm low birth weight is also considered a social problem. A study by Kang et al. [17] reported the ability of various strains of Weissella cibaria to decrease the production of volatile sulphur compounds by Fusobacterium nucleatum [18].

PROBIOTICS IN CARIES MANAGEMENT

Streptococcus mutants is the main causative microorganism in caries development because of its ability to produce highly branched, water-insoluble glucan, mutant, which facilitates its establishment in the oral biofilm. Its acidogenic properties and rapid metabolism of sucrose, fructose and glucose generates low pH that challenges the homeostasis in the oral microbial community with a shift towards bacteria that induce caries [19]. Moreover, elevated salivary counts of S. mutants are associated with higher caries risk and disease progression. It has been shown that Probiotic strains and putative Probiotic candidates suppress the growth of S. mutants and other oral streptococci with cariogenic potential [20].

PERIODONTAL DISEASES AND PROBIOTICS

The accumulation of bacteria within the biofilm, facilitated by poor oral health maintenance, predisposes to allogenic shifts in the microbial community, leading to the onset of periodontal inflammation [21]. Periodontal diseases are largely caused by specific gram-negative anaerobic bacterial infections, leading to the initial destruction of the soft connective tissue and, subsequently, to the disruption of the underlying alveolar bone and periodontal ligament. Oral biofilms are dynamically changing and develop increasingly complex structures as they mature. Interaction between species is characteristic in biofilms. Bacteria in the biofilms resist environmental stresses as well as antibiotics [22]. As such, Probiotic bacteria have to overcome a hostile environment for their survival and colonization in the oral cavity. Probiotic bacteria therefore, should show adhesive properties to bind with salivary proteins, saliva coated hydroxyappatite or oral epithelial surfaces. Auto aggregation and co aggregating properties of Probiotics also help these bacteria to establish themselves in the oral cavity. Haukioja et al. showed the binding of Lactobacillus and seven Bifidobacterium strains to hydroxyapatite and microtitre wells coated with human saliva [23].

PROBIOTICS AND CANDIDIASIS

Disequilibrium in microbiota can favour the growth of opportunist microorganisms and the development of pathologies, like candidiasis caused by yeasts of the Candida genus. Individuals presenting Candida in the oral cavity used the probiotics in the treatment and showed a significant reduction in Candida prevalence (46%) and mean Candida CFU/ml counts (65%). The Candida species identified were C. albicans (98%) and C. tropicalis (2%), before and after Probiotics consumption. Immunological analysis demonstrated a significant reduction in anti-Candida IgA levels after Probiotics use, probably due to less antigenic stimulation. Hence Probiotics use significantly reduced the amount of Candida in the oral cavity, possibly due to competition between the yeasts rather than by specific secretory immune response stimulation [24].

PROBIOTICS COMPENSATION FOR LACTASE INSUFFICIENCY

Yogurt and other probiotic bacteria in fermented and unfermented milk products improve lactose digestion and eliminate symptoms of intolerance in lactose maldigesters. These beneficial effects are due to microbial galactosidase in the (fermented) milk product, delayed gastrointestinal transit, positive effects on intestinal functions and colonic microflora, and reduced sensitivity to symptoms. Intact bacterial cell walls, which act as a mechanical protection of lactase during gastric transit and the release of the enzyme into the small intestine, are determinants of efficiency. Probiotic bacteria target the colon, normally promote lactose digestion in the small intestine less efficiently than do yogurt cultures [25].

PROBIOTICS AND ALLERGIC DISEASE

The studies by Kalliomäki and colleagues [26]. noted that lactobacillus (LABs) can shorten the duration of diarrhoea [27]. And increase rotavirus specific IgA [28]. And that this effect was dependent on live bacteria [29]. Experimental Rotavirus infection of normal and germ free mice increased intestinal permeability and the extent and timing of this increased permeability was altered by intestinal microflora [30]. Cow's milk protein is one of the first foreign proteins encountered in infancy. Infants who become allergic to cow's milk develop eosinophilic intestinal inflammation and increased gut permeability. This inflammation and increased permeability can be reversed by the addition of LABs to their diet. LABs have also been shown to enhance gut IgA responses to milk proteins in animal models [31].

ANTICHOLESTEROLAEMIC EFFECTS

The effect of yoghurt and acidophilus milk on blood cholesterol levels is variable. Feeding yoghurt to humans produced lower blood cholesterol concentrations (Mann 1977) but skimmed milk will also achieve the same result (Nair and Mann 1977). However, other work has shown that fermented milks give a lower serum cholesterol concentration than untreated milk (Grunewald 1982). The suggestion was that fermented milk contained bacterial metabolites which inhibit cholesterol synthesis by the body. However, some lactobacilli have a direct effect on cholesterol levels by assimilation and removal from the growth medium. Feeding trials showed that such organisms significantly reduced cholesterol levels in the serum of pigs fed cholesterol (Gilliland et al. 1985) [32].

HYPERTENSION

Two Japanese studies have been published on the effect of fermented milk on blood pressure. In the first study, Lactobacillus helveticus and Saccaharomyces cerevisiae were used, in the second one L. casei TMC 0409 and Streptococcus thermophillus TMC 1543 were investigated. In both studies significant reductions in systolic blood pressure were found, and in one study effects on diastolic blood pressure were also noted. It was suggested that the effect could be due to the formation of certain tripeptides that are inhibitors of ACE (Angio-tension-converting enzyme) [33].

EFFECTS OF PROATHEROGENIC AND PROBIOTIC BACTERIA ON MAST CELLS AND INFLAMMATION

Mast cells are immunological cells have host defense function, participate in the regulation of many other physiological functions of the body such as the regulation of tissue homeostasis, intestinal functions, and neuro-immune interactions, by producing multiple mediators including cytokines, chemokines, leukotrienes, prostaglandins, proteases, and biogenic amines. However, these same mast cell-derived mediators are involved in the pathogenesis of many inflammatory diseases, such as atherosclerosis and other metabolic disorders, as well as allergy and intestinal diseases. Probiotics have been under extensive study regarding their ability to modulate immunological functions and, thus, their possible benefits in the prevention and alleviation of inflammatory diseases [34].

ATOPIC DISEASE

The hygiene hypothesis conceives the rapid increase in Atopy to be related to reduce exposure to microbes at an early age as a result of constant and thorough hygienic practices, almost sterile food, vaccination etc. Probiotics administered prenatally and postnatally for 6 months to children at high risk of atopic eczema succeeded in reducing the prevalence of atopic eczema by half compared with that in infants receiving placebo. The precise mechanisms have not been elucidated, but the premise is based upon the ability of lactobacilli to reverse increased intestinal permeability, enhance gut-specific IgA responses, promote gut barrier function through the restoration of normal levels of microbes, and enhance transforming growth factor-β and interleukin-10 production as well as cytokines that promote the production of IgE antibodies [35].

PROBIOTICS AND ACUTE OTITIS MEDIA

Acute otitis media is the most common bacterial infection in young children. However, the increasing numbers of antibiotic-resistant pathogens, the risk of affecting the balance of the indigenous oro-nasopharyngeal microbiota (facilitating colonization with pathogens), as well as the costs and risks associated with tympanostomy tube placement, has led researchers to explore the possibilities of using Probiotics.The rationale for such an approach lies within the observation that children who are prone to acute otitis media harbour fewer α-haemolytic streptococci in the nasopharynx than children who are more resistant to acute otitis media. Additionally, some α-haemolytic streptococci have an interfering activity against pathogens that cause acute otitis media [36].

PROBIOTICS AND HIV

Recently the role of Probiotics to slow down the progression of AIDS (Acquired immunodeficiency syndrome) has been postulated by Lin Tao and colleagues (2008). A screening of saliva taken from hundreds of volunteers showed that some Lactobacillus strains produced proteins capable of binding a particular type of sugar, called mannose, found on HIV envelope. The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract and colonize them. One of the strain showed abundant mannose-binding protein particles into its surroundings which binded to the sugar coating and hence neutralized HIV. They also observed that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harboring HIV and prevent them from infecting other cells [37].

FUTURE PROSPECTIVE

Significant benefits in oral and general health on administration of Probiotics have been reported by many researchers. Probiotics have great potential as agents to improve or maintain a balanced intestinal micro flora to enhance overall health and general wellbeing. Future developments will attempt to discover more effective strains, Genetic engineering and the recombinant DNA technology can auxiliary improve the Probiotic characteristics which could be used in general health. In this way it would be possible to bring together the ability to survive in the gut and to produce the metabolites which are responsible for the probiotic effect. The probiotic acidogenic bacteria can be engineered genetically to put off dental caries. Mutations can be induced to craft the mutants with increased bacteriocin production. Such mutant strains displace the indigenous strains and colonize the oral cavity. Still many in vitro and in vivo tests for the presence of the desirable characteristics must be carried out and a range of random trials need to be performed to find out the most potent Probiotics organisms for overall health and the most valuable ways of their administration.

CONCLUSION

Probiotics represent a new area of research in various therapies. The existence of Probiotics in the indigenous oral micro flora of humans warrants exploration because these bacteria offer the advantage of being perfectly adapted to the human oral ecosystem. Probiotics are counterparts of antibiotic thus are free from concerns for developing resistance, further they are body's own resident flora hence are most easily adapted to host. With fast evolving technology and integration of biophysics with molecular biology, designer Probiotics poses huge opportunity to treat diseases in a natural and non invasive way. It can be said Probiotics are still in “infancy” in terms of health benefits, but surely have opened door for a new paradigm of treating disease on a nano – molecular mode. Much more scientific developments are needed to have a better understanding of these tiny forms of lives in order to broaden their potential applications. Probiotics have been analyzed for treatment and prevention of various diseases and disorders of human body and the results obtained are very encouraging. Probiotics have turned out to be very promising in ensuring oral health and general well being.

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