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In Silico Prediction and Evaluation of the Selected Microbial Strain with Prebiotic Properties

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***Abstract*—Probiotics are useful bacteria which helps the human body when taken in adequate amount to improve the overall health as well as prevention of various illnesses. Probiotics can be used in treating many diseases ranging from respiratory tract infections to gastrointestinal diseases. Lactobacilli species are omnipresent in the environment and they also play an important role in food and other industries. Besides the environment they are also part of intestinal, oral and vaginal microbiome. In this study we have considered the Lactobacillus casei BL23 strain and compared with the other majorly commercialized strains and found that they are almost similar to the former strain. The genome of the BL23 was sequenced using a combination of pyro-sequencing and short gun sequencing. The CRISPR array is identified by using the CRISPR finder tool. The present study analysed the genome completely for the presence of antibiotic resistance that acquired as a defence mechanism and tried to forward the study and apply it in the food safety. In-silico analysis of Lactobacillus casei BL23 genome sequence resulted in CRISPR as immune or defence mechanism against the foreign elements. There is only one array and 21 spacers. The genome sequence data clearly showed that there are no plasmids present in this strain. The result obtained suggested that Lactobacillus casei BL23 can be utilised in food industry as it facilitate its application as a probiotic or starter culture in food industries and considered to be save as it is free of virulence determinants.**

***Keywords*—CRISPR; Genome sequencing; Lactobacillus casei BL23 strain; Probiotic**

I. INTRODUCTION

In this modern era where the humankind is dealing with the hectic works, proper diet and nutrition is a key to maintain the health and fighting back the diseases. Safety and composition of foods gain higher importance because of the problems associated with the low-quality foods such as food allergy, food poisoning, cancer, obesity, etc. In this regard, Probiotics and Prebiotics came into existence. Probiotics means “for life” and they are live microorganisms, used to name associations of bacteria with their beneficial and positive effects on both animal and human health. Most probably, Probiotics were invented in 1954 by Ferdinand Vergin in one of his paper named “Anti- und Probiotika”. With the course of time, there are drastic modifications in the definition of probiotics. Probiotics’ new definition was proposed by Huisint Veld and Havenaar, which states probiotics as live mono or mixture of bacterial cultures affecting the host advantageously by ameliorating the characteristics of native flora, both when administered in humans or in animals (Havenaar & Huis In’t Veld, 1992). On the other hand, Prebiotics are defined as non- digestible substances which are beneficial for the host body by stimulating the activities or the growth of the bacteria present in the colon. It was proposed in 1995 earliest by Marcel Roberfroid and Glenn Gibson and this definition remains unaltered from 15 years. But in 2008, according to the International Scientific Association of Probiotics and Prebiotics (ISAPP), “dietary prebiotics” are defined as particular fermented ingredients with which some particular changes can be made in the activity and composition of the gut microbiota, thus possessing beneficial effect(s) to the health of host (Davani-Davari et al., 2019). There are variety of probiotic strains used commonly in the form of active cultures of live bacteria. Some of the common bacterial genus used as probiotics are Lactobacilli, Bifidobacteria, Lactococci, Streptococci. Specific species of these Lactbacilli genera are (L. plantarum, L. gasseri, L. reuteri, L. casei, L. rhamnosus, etc.), Bifidobacteria genera are (B. bifidum, B. longum, B. animalis, etc.), Lactococci genera are (L. acidophilus, L. lactis, L. curvatus), Streptococci genera are (S. oralis, S. salivararius, S. thermophilus)(George Kerry et al., 2018). Some of the Prebiotics includes oligofructose, insulin, variety of oligosaccharides such as, xylose- containing, and galactose- containing, fructo- oligosaccharide processed from sucrose(Hutkins et al., 2016). Commercial probiotic products available in market are Actimel (L. casei DN114001), Yakult (L. casei Shirota), Actifit (L. rhamnosus GG), ProViva (L. plantarum 299v), LC1 (L. johnsonii La1)(Saxelin et al., 2005), Biopron 9 (B. bifidum, B. longum, B. breve), 4lacti (S. thermophilus), Asecurin (L. reuteri, L. gasseri, L. rhamnosus). There are more probiotic products available in market like Oslonka Normal, Biotyk, Dicoflor, Trilac, Lacidofil, Lakcid, BioGaia, etc.(Korona-Glowniak et al., 2019).

II. PROBIOTICS AND IMMUNE SYSTEM

Probiotics, being prokaryotic microorganisms, are having multitude of advantages for eukaryotic human being. The colon

present in the human intestine comprises of millions of bacterial strains which outreach the number of cells constituting the human body. These bacterial colonisation starts dwelling in the gastrointestinal tract when the foetus is developing in the mother's womb and the first encounter with the bacterial species get from mother's intestinal and vaginal source. Other sources after birth includes breast feeds (primarily Bifidobacteria), or feeds based on formula (providing complex set of organisms composed of Clostridia, Enterobacteria, Bifidobacteria, Lactobacilli, Streptococci, and Bacteroides) (Limdi et al., 2006). These strains, also termed as gut microbiota, are responsible for maintaining the positive environment in the gastrointestinal tract and any activity in this region generates immune response. Any encounter of pathogenic bacteria, introducing in the body from environment or contaminated food, causes disturbance in the intestinal biota. In such situations, Probiotics with advantageous properties will not only balances the environment of intestine but also counteract the pathogenic bacteria from invading the mucosal barrier. Most of the recent studies confirm the probiotics effectiveness against the gastrointestinal diseases (such as infectious diarrhoeas, inflammatory bowel syndrome, H. pylori suppression, inflammatory bowel disease) and some allergic diseases like atopic der- matitis (Markowiak & Ślizewska, 2017). After the meta- analysis of 11 probiotic strains, they have been concluded that these are efficient in preventing 8 considerable GI tract diseases, the antibiotic- associated diarrhoea, infectious diarrhoea, Clostridium difficile infection, Inflammated bowel syndrome, pouchitis, Helicobacter pylori infection. There has been noted that in these con- cluded strains was shortage of efficacy for necrotizing enterocolitis and traveler's diarrhoea (Khalighi et al., 2016). The effects of probiotics on numerous diseases have motivated various studies for testing the therapeutic benefits. Some of the results showed the probiotics to be effective against IBD at a less severe stage by targeting the regulation of T cell response in the intestinal mucosa, this response can be subjected to the overwhelming inflammatory response. Several other studies, based on controlled, randomized probiotics trials, concluded that ulcerative colitis has amenable effects upon the treatment by probiotics than Crohn's disease. In a study, treating with single organism as probiotic, Lactobacillus johnsonii, administered orally, Crohn's disease re- occurrence after surgery was prevented. In the recent studies, effect of mix of probiotic strains, VSL#3 was partially effective on T- cell regulation, TNBS (trinitrobenzene sulphonic acid) colitis, Th 1- mediated colitis. Whereas, Lactobacillus casei was seen to be more positively effective on the experimental inflammation (Boirivant & Strober, 2007). These studies open a way for more research on the effectiveness of probiotics in the treatment of several diseases.

III. MECHANISM OF ACTION OF PROBIOTICS

There is a misconception regarding the common action of probiotics by colonizing the intestine. However, some strains of probiotics such as B. animalis and Lactobacillus casei may not colonize in the intestinal tract, rather they would exert their action indirectly, either by passing through in a transitory way or by impacting the existent microbes. Few examples of this are Saccharomyces boulardii present in the intestine of mice showed indirect, non- mucosal adhering colonization and was only distinguishable for 2-5 days after the treatment termination. This was detected not to involved in altering the total number of bacteria or any number of considerable groups of bacteria. Even S. boulardii was resistant to antibiotic treatment as it can help to restore the healthy count of microbiota and regained the normal biota more rapidly than control animals. One more example includes the transitory colonization of Lactobacillus rhamnosus RD20 which was only detectable for the specific period of consumption in the faeces of 6 volunteers of human. However, this strain of probiotic did change the number of enterococci and lactobacilli in the faecal sample, yet only in the course of treatment period (Ohland & MacNaughton, 2010). This non- colonization was one out of the many ways of action of probiotics. This section of the review will cover the mechanism of probiotics and their effects on some main regions of human intestine. Probiotic effects on Epithelial barrier: To enhance the epithelial integrity and to provide the protection to microorganism from the surroundings, the intestinal barrier plays a major defensive role. The defences of this barrier include antimicrobial peptides, mucosal layer, epithelial junction complex and secretory IgA. But, once these barriers got disrupted, the foreign bacterial and food pathogens may approach the submucosa and might produce inflammatory responses and hence result in gastrointestinal disorders such as Inflammatory Bowel Disease (IBD). For the maintenance of this barrier and to prevent foreign microbes to invade, some non- pathogenic species of live bacteria or yeast can come up with relevant action. Probiotics are extensively studied to maintain the epithelial barrier. The mechanisms with which probiotics perform are still in progressing research. Different studies have shown that by enhancing the genes' expression, which are responsible in signalling of tight junction, is a feasible mechanism to strengthen the intestinal barrier integration (Bermudez-Brito et al., 2012). Recent findings have shown probiotics as the initiators for repairing the function of barrier after damage. As in the case of Escherichia coli Nissle 1917; it not only prevents the mucosal barrier disruption by pathogenic E. coli, but also reimpose mucosal integrity in CaCo-2 (derived from human colon carcinoma) and T84 cells (Zyrek et al., 2007). This effect is being generated by increased expression and reorganising of proteins present in tight junction such as PKC (protein kinase C) and zonula occludens (ZO- 2) which leads to the repairing of tight junction complex (Stetinová et al., 2010). In a recent paper on the probiotics function in epithelial barrier, it has been reported that

VSL#3 (mixture of prebiotics and probiotics) is also working with same mechanisms of supporting the function of intestinal barrier. It protects the barrier and elevates the expression of tight junction protein by stimulating the pathways of signalling through Extracellular regulated kinase (ERK) and p38 (mitogen- activated protein kinase) both in in vitro and in vivo studies (Dai et al., 2012). Probiotic effects on mucosal adhesion: The intestinal epithelium contains glycoproteins and glycolipids, together constituting glycocalyx layer, which provides protection from any bacterial infections and mechanical damage. The mucosal layer consists of mucins (glycosylated proteins), immunoglobulins, glycolipids, and elec- trolytes. Glycosylated proteins, i.e., mucins have ligands in the form of sugar residues which will provide receptors for bacterial binding (Monteagudo-Mera et al., 2019). There are several surface molecules present in most used probiotic species (Lactobacil- lus and Bifidobacterium). These species having surface layer proteins (SLPs), mucin- binding proteins (Mubs) and lipoteichoic acid (LTA) which plays a crucial role in interacting with the components present in the mucosal layer (Lebeer et al., 2010). Mucin-binding proteins are adhesive proteins consisting of mucus- binding (Mubs) as well as mucin- binding proteins (MucBP). These are extensively present in gastrointestinal tract of humans and in several species of bacteria but particularly in lactic acid bacteria isolated from human gut (van Tassell & Miller, 2011). Some more adherence components are pili or fimbriae which are present in Gram- negative as well as Gram- positive bacteria (like Bifidobacteria). Some Lactobacillus species produces SpaCBA pili, which was first characterized in Lactobacillus rhamnosus LGG, helps in providing this probiotic strain with high adhesion property (Monteagudo-Mera et al., 2019). On the other hand, SLPs has been observed to be the essential component for the adhesion to the mucosa and after removing it with chemical treatment, the reduction in the adhesion was noticed (Zhang et al., 2013). These surface layer proteins, if present in a probiotic bacteria, play a role of immunomodulator factor and pro- duce immunological responses by interacting with the host receptors in intestine (Konstantinov et al., 2008). Probiotic effects against pathogenic microorganisms: The microbial colonization in the intestine is a complex biota and when new organisms are introduced in this ecosystem leads to the high competitiveness among the microorganisms. However, those organisms which can be able to produce some substances able to compete with the existing organisms will be at an advantage. These substances are thus known as antimicrobial substances. Different studies shows that probiotic strains produces antimicrobial substances which helps in the improvement of resistances of colonization on the urogenital tract, gastrointestinal tract, and respiratory tract (Nag- pal et al., 2012). There are numerous antimicrobial substances which are produced by various probiotic strains. For example, Lactobacillus brevis 925A produces bacteriocin named as brevicin 925A which was found effective against the cause of dental caries and food poisoning caused by Streptococcus mutans and Listeria monocytogenes. Alike bacteriocin substances were also recognized in Lactobacillus plantarum TMW1.25 (Wada et al., 2009). Other examples include Lactobacillus johnsonii NCC 533 contains antimicrobial substances which were able to reduce the number of Salmonella typhimurium in vitro and in vivo. This antimicrobial activity is linked with the production of hydrogen peroxide and lactic acid (Liévin-Le Moal & Servin, 2014). When samples from oral mucosa was collected from 16 individuals, it was observed that 20 isolates were collected and two among them was identified as Lactobacillus casei G3 and Lactobacillus plantarum G1. These isolates exhibit the bacteriocin ability which were able to inhibit the growth of pathogenic organisms such as Pseudomonas aeruginosa, Staphylococcus aureus, Clostridium sporogenes, Salmonella abony and Escherichia coli, also these bacteriocins have enhanced lipid metabolism, without toxicity and vitality in the gastrointestinal tract(Zavisic et al., 2012). Probiotics effects on the immune system: The gut microbiota influences the immune system maturation and modulation during early postpartum period. The onset of diseases can be characterized by some dysregulation in the immune system like inflammatory disorders, allergies, autoimmune disorders and some infections. The modulation in the immune system can be done by the gut microbiota by pro- ducing the specific molecules responsible for the anti- inflammatory and immunomodulatory functions. The immunomodulatory functions are because of the probiotic bacteria interacting with the dendritic cells (DCs), intestinal epithelial cells (IECs) and with lymphocytes (B- and T- cells) and macrophages or monocytes (D'Amelio & Sassi, 2018). The gut microbiome produces diverse metabolites by introducing the modification in the host products and from digested food, short chain fatty acids (SCFAs) are among these metabolites which are mostly studied for the immune system and inflammation modulation. These SCFAs are in- vestigated to be generating anti- inflammation effects on the intestinal mucosa and hence protecting the intestine from developing various inflammatory disorders (Smith et al., 2013). Other than these SCFAs as metabolites, there are probiotic bacteria exerting their modulating effects on the host intestinal immunity and they perform their actions through different mechanisms. One of the mechanisms of action is to regulate the immune response in the host body by probiotics. Innate and adaptive immune systems are the two constituents of the immune system, in which adaptive immunity mainly depends on the T and B lymphocytes, and innate immunity is more related to structures, present in major group of pathogens, known as Pathogen- Associated Molecular Patterns (PAMP). These PAMP structures are having the sites on which PRRs (Pattern Recognition Receptors) bind and gener- ating the primary response to the pathogens (Plaza-Diaz et al., 2019). PRRs constitute Toll-like receptors (TLRs), Nucleotide- binding Oligomerization domains (NOD)- like receptors (NODLRs), lectins and adhesion molecules (Claes et al., 2015). TLRs are the transmembrane

proteins which are exhibited in both immune and non- immune cells like NK (Natural Killer) cells, B cells, Dendritic cells, epithelial cells, endothelial cells and fibroblast. The TLR recognizes certain components of microbes and producing the T-helper 1 (Th1) cells and T- reg cells (regulatory T cells) (Gómez-Llorente et al., 2010). Introduction of the pathogenic microbes in the host may disequilibrate the interaction between host and the microbes introduced. This leads to the diminished immune response and it can be corrected by the probiotics which will help in preserving the intestinal homeostasis and producing the T- reg cells, thus enhancing the immune response (Yousefi et al., 2015).

Probiotics and Auto- immune diseases: Auto immune diseases are caused by the imbalance in the immune system, but the pathogenesis is not well understood. Instead, some genetic histories and environmental factors (infections, diet, drugs, etc.) have been proposed in most of the research (De Luca & Shoenfeld, 2019). Above mentioned sections give the overview about the mechanism of action of probiotics and includes some examples in which these are modulating the immune system, thus preventing the diseases. There are several probiotic strains which can control the immune responses and modulate the immune system of the host at mucosal level. These probiotic bacteria, along with stimulating the foreign pathogenic bacteria from invading into the host immune system, mediate the auto- immune disorders such as Rheumatoid arthritis, Inflammatory Bowel Diseases, Multiple Sclerosis, Systemic Lupus Erythematosus, Type 1 diabetes and more (Dargahi et al., 2019). The role of probiotics in different auto- immune diseases is shown below in the table.

Auto- immune diseases Probiotic strain Mechanistic action References Type 1 Diabetes Bifidobacteriaceae, Streptococcus thermophilus, Lactobacillaceae, Lactobacillus johnsonii N6.2 It generates protolerogenic environment in intestine along with increased expression of IDO (Indoleamine 2,3- dioxygenase) and decrease in expression of IL- 1β (inflammatory factor). Provides enhancement of gut environment and thus modulate pathogenesis of Type 1 diabetes. It increases tryptophan level in serum and effector Th1 cells and cytotoxic T- cells. Responsible for the reduction of Type 1 diabetes occurrence risk. (Dolpady et al., 2016)(Marcial et al., 2017) Rheumatoid arthritis Lactobacillus casei Reduces pro- inflammatory cytokines (TNF-α, IL- 12 and IL-06) and alleviates the (Interleukin-10) regulatory cytokine, thus decreases the rheumatoid arthritis activity. Systemic Lupus Erythe- matosus (SLE) Bifidobacterium bifidum LMG13195Clostridia, Blautia coccoides DSM935, Ruminococcus obeum DSM25238 Prevents over activation of CD4+ lymphocyte. Remarkable drop in IFNγ/IL- 17 (Th1/Th17) and promotes the regulatory T- cells (T- reg cells). (López et al., 2016) Inflammatory Bowel Disease (IBD) Lactococcus lactis ML2018 Lactobacillus casei Shirota Possesses anti- inflammatory effect in vitro and in vivo using LPS (Lipo-Polysaccharide)-induced and DSS (Dextran Sulfate Sodium)- induced models. It prevents the inflammation by inhibition of MAPK (Mitogen-Activated Protein Kinase) and NF-κB activation. Increases the production of IL-4 and decreases the secretion of IFN-γ and IL-22 observed in samples of dendritic cells from Ulcerative colitis patients. It restores the normal stimulation capacity by reducing TLR4 and TLR2 expression. (Liu et al., 2019) (Plaza-Díaz et al., 2017) Multiple Sclerosis (MS) L. casei, B. bifidum, L. reuteri, L. acidophilus, Streptococcus thermophilus It inhibits the Th1/ Th17 pro- inflammatory response while generates the production of IL-10 and T- reg cells. Delays the onset of the disease.

IV. HEALTH BENEFITS OF PROBIOTICS

Probiotics have appeared to give an diverse assortment of medical advantages to human, creature, and plans. In any case, practicality of the microorganisms all through the preparing and capacity assume a significant part in moving the guaranteed wellbeing impacts. Along these lines, the medical advantages should be reported with the particular strain and explicit dosage.

Health of humans-

Medical advantages of probiotic organisms are very strain explicit; along these line. In the case of probiotics. None of the strains are totally relevant with the beneficiaries which are thought of to be getting by it. We never get the desired result from species which are similar in function , there are some or the other health imbalances with the species used. The medical advantage of fermented food varieties might be additionally improved with the help of addition of the different species in the probiotic medicines(Markowiak & Śl- izewska, 2017) produced. Different species include lactobacillus,, acidophilus, and bifidobacterium species. What's more, L. casei species are the most utilized probiotic societies with set up human well-being. In industries such as dairy, there are a different sets of species which are used for the preparation of different products and also for preparing probiotics . species such as bacillus subtilis, escheresia coli or the sacchromyces cerevisiae.

A few investigations have recorded probiotic impacts on diversity of gastrointestinal including anticipation and easing indica-tions of traveller's disease and anti-microbial related the diseases, fiery gut diseases, lactose bigotry, assurance against intestinal diseases, and irritable disorder. A few probiotics have likewise been examined (Morshedi et al., 2019) comparable to lessening commonness of atopic skin inflammation, vaginal diseases, and insusceptible improvement, adding to the inactivation of microbes in the gut, rheumatoid joint pain, improving the invulnerable reaction of in old people, and liver cirrhosis. probiotics are proposed to help the body's nomally working gut microbiota. Some probiotic arrangements have been utilized to forestall

diarhoea brought about by anti-toxins, or as a component of the treatment for anti-microbial related dysbiosis. In spite of the fact that there is some clinical proof for the job of probiotics in bringing down cholesterol yet the outcomes are clashing. Probiotics have a promising inhibitory impact on oral microorganisms particularly in adolescence yet this may not really lead to improved oral wellbeing. Antigenotoxicity, antimutagenicity and anticarcinogenicity are significant likely utilitarian properties of probiotics, which have been accounted for as of late. Observational information propose that utilization of aged dairy items is related with a lower pervasiveness of colon disease, which is recommended that probiotics are fit for diminishing the danger of malignant growth by restraint of cancer-causing agents and favorable to cancer-causing agents, hindrance of microscopic organisms fit for changing supportive of cancer-causing agents over to cancer-causing agents. The more helpful the microorganisms and organisms are, the more "rich" the soil is. These microorganisms separate natural matter in the soil into little, usable parts that plants can take-up through their underlying parts suvh as roots. The better the soil, the lower the requirement for engineered herbs/pesticides and fertilizers. The idea that specific microorganisms 'probiotics' may give direct benefits to the plant going about as biocontrol specialists for plants. The plant probiotic microscopic organisms have been detached and monetarily produced for use in the natural control of plant sicknesses or biofertilization. These microorganisms have satisfied significant capacities for plant as they offend different plant microbes, actuate resistance, or advance development. The communication among microbes and parasites with their host plants has shown their capacity to elevate plant development and to stifle plant pathogens in a few examinations.

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V. THE ROLE OF PROBIOTICS IN PREVENTION AND TREATMENT OF DISEASES

Probiotics are nothing but the useful bacteria which helps the human body when taken in adequate amount to improve the overall health as well as prevention of various illness. Probiotics have the capability to regenerate our digestive system with useful microbes that will counteract with the harmful bacteria.(Liu et al., 2018) Even though the incorporation of probiotics in human diet is there from many years it took so long to acknowledge the fact that they have threptic effects. Since then, the probiotic studies have become more prominent in treating various diseases. Probiotics can be used in treating many diseases ranging from respiratory tract infections to gastrointestinal diseases.(Liu et al., 2018). However the diseases which have certain level of evidences that probiotics can support them in prevention are gastrointestinal diseases and auto immune diseases. Despitehe evidences for the efficacy there is no proper research which explicitly state the threptic properties. The three species which were used extensively in the threptic studies of probiotics are Lactobacillus, Bifidobacterium and Saccharomyces. (Reid, 2016)

A. Gastrointestinal Diseases

Probiotics are widely used in treatment of gastrointestinal diseases. The diseases which have evidence that taking probi- otics are effective for acute infectious diarrhea, irritable bowel syndrome, functional gastrointestinal disorders, ulcerative colitis, hepatic encephalopathy, necrotizing enterocolitis, traveler's diarrhea.(Amara & Shibl, 2015)

B. Acute Infectious Diarrhoea

Acute diarrhea is categorized as the disease in which there are more than often bowel movements which last 10 to 14 days. The transmission of this disease is usually fallows oral route ie) contaminated hands, food, or water. The main reason of this ailment are viral infections, bacterial infections and parasitic infections. The probiotics of proven efficacy such as Lactobacillus casei , Saccharomyces boulardii can be used in order to treat the acute infectious diarrhoea in children by warning against the possible antibiotic resistance. There are many studies which have conducted in various countries have shown positive results after administered probiotics in case of this disease they are reduction in number of stools in given time ; regain in lost body mass in infants ; reduction of risk and average duration of diarrhoea. By summing wup all the results in various studies conducted it is considered that the administration of probiotic in infectious diarrhoea gives them many advantages compared to the control group in every study. In many cases S.boulardii is administered and it effectively shortens the average diarrhoea duration by 17-30 hours.(Collinson et al., 2020)

C. Irritable Bowel Syndrome

Irritable bowel syndrome is one of the most common gastrointestinal diseases seen all over the world. Irritable bowel syn- drome is a disease which is characterised by abdominal pain and pain during defecation. This usually occurs mostly in adult population mainly women. The main reason for the occurrence of this disease is malfunction of intestinal microflora which actually results in poor absorption of bile acids in the colon while increasing fluid and mucus secretion through the mucosa which end up in diarrhoea. The main problem lies here is malabsorbtion of bile acids so the bacterial species related to the genus Lactobacillus and Bifidobacterium are involved in the conjugation of bile acids which lowers the acid that reaches the large bowel and this leads to reduce the extent of diarrhoea and may comfort the patient. There are many clinical trails which used

Lactobacillus plan- tarum 299 v(Lp 299 v) in case of IBS has reduced the symptoms associated with it such as abdominal pain, painful defecation and bloating. As irritable bowl syndrome is chronic disease probiotic administered daily for one month has significantly showed 20% improvement compared to the control group of the experimental study. Along with Lactobacillus plantarum, lactobacillus rhamnose and B. infantis 35,624 is also found useful in treating the irritable bowel syndrome.(Wilkins et al., 2017)

D. Antibiotic- Associated Diarrhoea

Antibiotic associated diarrhoea is a condition which is occurred as a side effect in uptake of antibiotics to other medical illness or infections. This condition usually occurs mostly in children and also adults. The two main causes of antibiotic associated diarrhoea, one of which is because of antibiotics or the drugs which we consume often leads to the changes in the intestinal microflora and its composition and also proliferation of bacterial strains resistant to the antibiotics and the other is deterioration of fermentation process by intestinal microflora. To prevent this disease, doctors advise to take the probiotics along with the antibiotic course and one week fallowed by the antibiotics. The probiotic bacteria which are proven to prevent the antibiotic-associated diarrhoea are Lactobacillus rhamnosus and Saccharomyces boulardii. In a clinical study conducted by Hickson et al. patients who are on ongoing antibiotic therapy has taken Actimel yogurt twice a day for a week has resulted a lower risk of antibiotic associated diarrhoea and diarrhoea caused by C. Diffle infection compared to the patients who have not taken the probiotic. The strains which have greater efficacy in preventing this disease are Saccharomyces boulardii and Lactobacillus GG.(The Therapeutic Effect of Probiotic Bacteria on Gastrointestinal Diseases Rola Probiotyków w Profilaktyce i Leczeniu Chorób Przewodu Pokarmowego, n.d.)

E. Constipation

Constipation is a condition where the bowel movements can be infrequent or hard to pass the stools. The stool of the patients who have Constipation is often hard and dry. The symptoms are abdominal pain, bloating and constant urge to defecate. Complications from Constipation may include haemorrhoids anal fissures or faecal impaction.

Uptake of probiotics in children as well as adults with Constipation has effective results. The probiotic should be administered daily with the onset of symptoms till the symptoms persist in them. There are many clinical studies which proved that adults with idiopathic constipation reported an increase in the mean number of stools per week after taking probiotics compared the control group , the similar kind of study conducted in children also improved the number of stools in a week after consumption of Bifidobacterium containing yoghurt. In both these cases probiotics has a greater threptic affect in patients with constipation to reduce their symptoms like defecation frequency, painful defecation and abdominal pain.(Amara & Shibl, 2015)

F. Probiotics and its use in Aquaculture

The process of breeding, raising, and harvesting of fish, shellfish, and aquatic plants is termed as aquaculture. In the recent studies it has been found that the usage of probiotic supplements in aquaculture is not only beneficial to the disease control but now improving the fish growth and reproduction as well . Probiotics can act as nutrient sources and providing the enzymes for better digestion and also modulating the immune system and increasing the immune response against the pathogenic bacteria. (The Role of Prebiotics and Probiotics in Aquaculture, n.d.)The most common probiotics which are used in aquaculture are lactic acid bacteria such as Lactobacillus species Bacillus species and Enterococcus species and yeasts such as Saccharomyces cerevisiae. As the probiotic supplementations is given to the water body the fish or any other organisms these can be able to modify

TABLE I

Disease or clinical condition	Probiotic organisms used as threptic measure.	
Irritable bowel syndrome	Bifido bacterium, Enterococcus, lactobacillus. Lactobacillus casei , Saccharomyces boulardii	Brenner and Chey, 2009, Enck et al., 2009 (Cameron et al., 2017)
Acute infectious diarrhoea	Saccharomyces boulardii,	(Probiotics for Gastrointestinal Conditions: A Summary of the Evidence - American Family Physician, n.d.)
Antibiotic associated diarrhoea	Lactobacillus rhamnosus, Bifidobacterium	(Shi et al., 2016)
Constipation		

the gut microflora and replace the harmful or detrimental microbes with the beneficial ones by competitive exclusion, as we are

populating the gut with live bacteria ,these exogenous bacteria compete with the pathogens already present inside the Organism and preventing their addition to the intestinal wall and limited access to the nutrients and secreting antibacterial substances such as bacteriocins and organic acids leads to the death of pathogenic bacteria .(Irianto & Austin, n.d.).

V. CONCLUSION

The employments of probiotics and their applications have shown enormous expansion over the most recent twenty years. Probiotics can turn numerous medical advantages to the human, creatures, and plants. Utilizations of probiotics hold numerous difficulties. Notwithstanding the practicality and tactile acknowledgment, it should be remembered that strain determination, preparing, and vaccination of starter societies should be thought of. Probiotics industry likewise faces difficulties while asserting the medical advantages. It can't be accepted that essentially adding a given number of probiotic microscopic organisms to a food item will move wellbeing to the subject. To be sure, it has been shown that practicality of probiotics all through the capacity period notwithstanding the recuperation levels in the gastrointestinal parcel are significant elements. For this reason, new investigations should be completed to: test fixings, investigate more choices of media that have not yet been modernly used, reengineer items and cycles, and show that lactose-bigoted and vegan purchasers request new feeding and attractive probiotic items.

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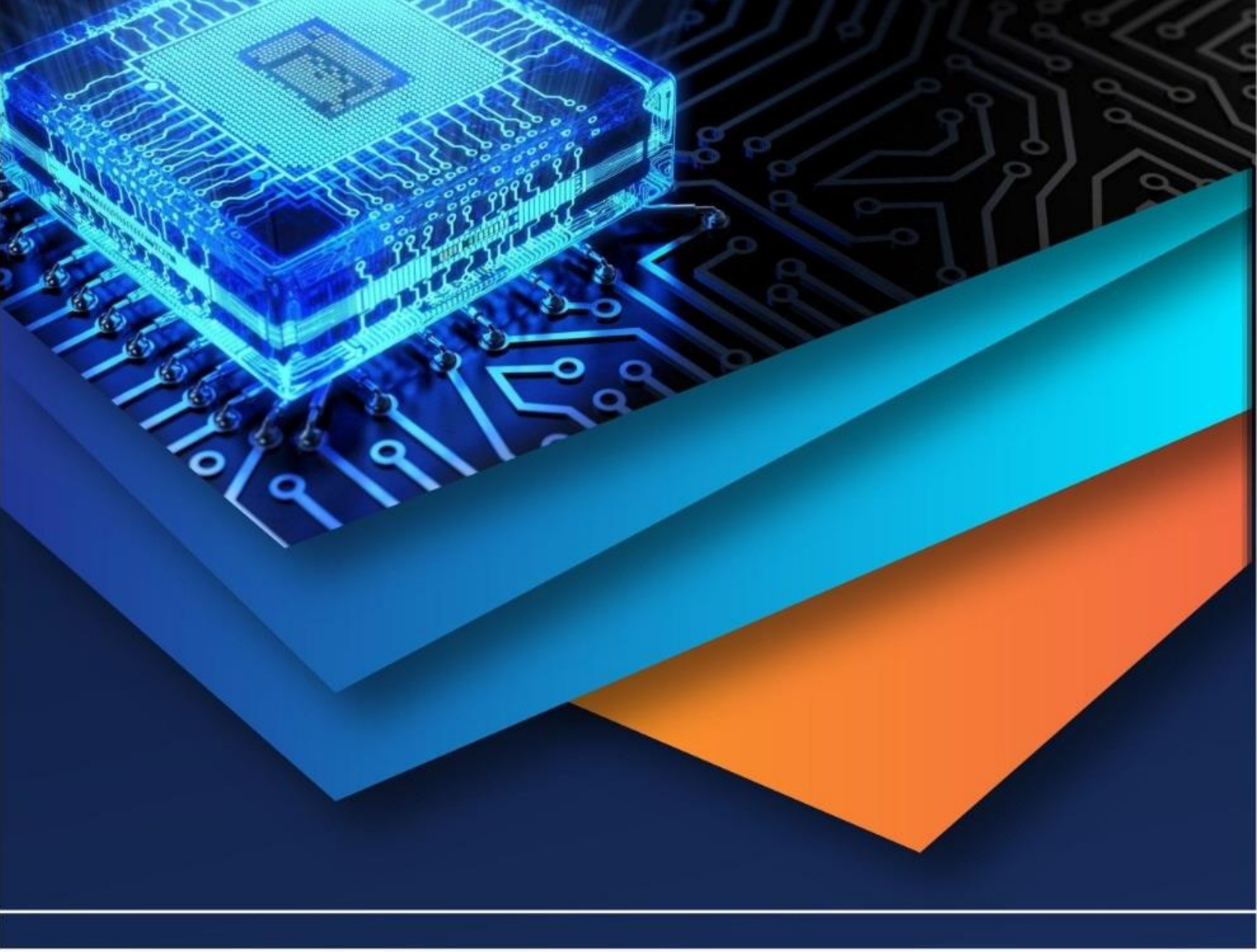

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