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PROBIOTICS: A SIGNIFICANT APPROACH TO HEALTH

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Abstract— **This report deals with the study that Probiotics have been with us for as long as people have eaten fermented milks, but their collaboration with health benefits have only come in the century when Metchnikoff gave idea of replacing dangerous microbes by useful ones in order to modify our gut flora. Later based on assumption that colonization of the gut was essential, used intestinal strains of Lactobacillus acidophilus for treatment of constipation, digestive hazards. According to Food and agriculture organisation of United Nations (UN) probiotics are live microorganisms which on administering in proper amount produces useful effects to the host when consumed orally. Probiotics were found to effectively influence the host by enhancing their microbial balance of intestine, thus suppressing pathogens and toxin forming bacteria.**

Hence, probiotics with boosting the functioning of the immune system also naturally help in fighting bad bacteria by providing the body with sufficient good to keep the body in symbiosis. It doesn't have any risk of overdose too that leads to the need for a prescription or the monitoring of a physician.

Keywords— **Probiotics, Gastrointestinal microbes, Gastrointestinal Tract, Lactic acid bacteria, Temperature, colon, Bifid bacterium sp., Epithelial barrier, Pathogen, Cytokine, Ant allergic, gut-bacteria imbalance.**

I. INTRODUCTION

Probiotics are living microorganisms which are important to provide good health when consumed, generally by improving or restoring the gut flora (Gibson et al. 1995; Jain et al., 2014). Probiotics improves the intestinal tract by supplying digestion enzymes, reducing pH, and by increasing the activity of enzymes in the gastrointestinal tract (Duggan et al. 2002). The most common probiotics presently used are belong to the genera Bifid bacterium and Lactobacillus (Ezendam et al., 2006).

The benefits of probiotics include the decrease of pathogenic gastrointestinal microorganisms, the reduction of gastrointestinal problems, to increase the immunity, helps in maintaining the skin, production of antibody against pollen allergens, the decrease in count of body pathogens, protection of DNA, the protection of lipids and proteins from damage due to oxidation, and the maintaining of intestinal microbiota while receiving antibiotic treatment. The word "probiotic" (from the Latin pro and the Greek word β□ ΌΩ literally meaning "for life") was introduced by the German scientist Werner Kollath, which means- "active substances which are essential for the healthy development of our life", the term "probiotics" was used by Lilly and Stillwell which means - "substances which are secreted by one organism which stimulate the growth of another microorganism" (Mc Farland et al., 2015).

The modern history of probiotics started at the beginning of the year1900s with the studies and research of a Russian scientist Elie Metchnikoff. She was working at the Pasteur institute in Paris. Louis Pasteur discovered the microorganisms which are responsible for fermentation, whereas Metchnikoff tried first to observe the effects of these microbes on human. He took a survey of Bulgarian rural people to the regular consumption of fermented dairy products such as yoghurt as they live long (Diplock et al. 1999). He linked this to the Bulgarian bacillus which was discovered by a 27 years old Bulgarian Physician Stamen Grigorov, and he later suggested that lactobacilli might counteract the commonly accepted effects of GIT metabolism contributed to illness and ageing (Holzapfel et al. 2001; Kechagia et al. 2013)

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Table 1: Microorganisms considered as probiotics

Lactobacillus sp.		
Name	**Uses**	**References**
L. acidophilus	L. acidophilus are used in many dairy products, sometimes in the production of acidophilus-type yogurt, or acidophiline.	Chukeatirote et al. 2003
L. reuteri	L. acidophilus are used in many dairy products, sometimes in the production of acidophilus-type yogurt, or acidophiline.	Mu et al.2018
L. rhamnosus	L. rhamnosus are useful in treating female-related infections, most particularly used in treatment of bacterial vaginosis (or "BV").	Cribby et al., 2008
Bifidobacterium Species		
B. animalis	B. animalis is mostly found in dairy products.	Kuru et al., 2022
B. bifidum	B.bifidum helps to cure infection by Helicobacter pylori, irritable bowel syndrome (IBS), restoration of intestinal bacteria after chemotherapy, constipation, etc.	O'Callaghan et al., 2016
B. breve	B.breve have been used to treat a number of conditions including constipation, diarrhea, and even the cold and flu.	BozziCionci et al. 2018

Other Lactic Acid Bacteria

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Enterococcus faecalis	Enterococcus faecalis, are used in probiotics to treat diarrhea and improve host immunity.	Araújo et al., 2013
Lactococcus lactis	Lactococcus lactis used in the food fermentation industry and its first genetically modified organism to be used alive for the treatment of human disease.	Song et al., 2017
Pediococcusacidilactici	Pediococcusacidi lactici used occasionally in dairy products in form of bio yogurt, where the culture is used for acidification and health reasons.	Barbosa et al., 2015
Non-Lactic Acid Bacteria		
Saccharomyces cerevisiae	Saccharomyces cerevisiae are widely used as a low cost and efficient adjuvant against gastrointestinal tract disorders such as inflammatory bowel disease.	Fernandez-Pacheco et al., 2018
S. boulardii	Saccharomyces boulardiiis most commonly used as medicine for treating and preventing diarrhea, including infectious types such as rotaviral diarrhea in children.	Erdeve et al., 2004

II. HABITATION OF PROBIOTICS BACTERIA

- The gastro-intestinal tract is the favourable place for probiotic bacteria, they can easily grow there with suitable environment, by directly adding live microorganisms which can balance gut microflora by diet. They made the GI tract healthy (Sornplang et al., 2016)
- Intestine contains lots of living microorganisms which constitute intestinal microflora. Our gut microbiota is mainly shaped across the lifetime through the diet which is considered as one of the main drivers. This microbiota gives many benefits to host body through physiological function. Immune and metabolic homeostasis maintained by intestinal bacteria and it also protects us against pathogens and harmful organisms (Fuller et al., 1992).
- Small number of microorganisms can be found in Stomach and very small amount in Colon but Lactobacillus, Bifid bacterium or Saccharomyces boulardii some of the most researched probiotics are stayed in stomach, some of anaerobes are found in colon (Soccol et al., 2010)

III. FACTORS AFFECTING PROBIOTICS

A. Physical Factor

Probiotic survival is mainly affected by physical factors like storage, temperature, drying conditions or oxygen levels (Vuyst et al., 2008). These factors are very required to their acceleration. Probiotics cell membrane get damaged because of mechanical stresses that is caused during freezing process

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set by the development of ice crystals in the external medium or inside the cells. By applying rapid freezing small ice crystals are formed for short time period (Fowler et al., 2005).
The fermentation temperature influences the durability of probiotic microorganisms; the majority of lactic acid bacteria are grown within a range of 30–43°C, this is their optimum temperature range. Some bacteria like those of yogurt cultures and L.acidophilus easily grow at 45°C. Usually, temperatures above 45 °C hinders probiotics during processing, this temperature causes negative effect on them (Lee et al., 2009). Bifid bacterium recognizes from the human intestinal tract such as B.longum subsp. infantis, B.breve, B.bifidum, and B.adolescentis, they have shown an optimum growth temperature in the range of 36–38 °C, but in case of B.animalissubsp.lactis can grow at higher temperatures of 41–43°C (Santivarangkna et al., 2006; Schutyser et al., 2012).Culture preservation methods (freeze drying) influence the formation and permanency of probiotic cell effector molecules. The prob-ability of probiotic functionality changes in response to culture processing steps that is proved by numerous studies. Processing and preservation affect the stress tolerance level of probiotics (Schutyser et al., 2012).
In order to keep cultures for experimental and industrial uses, drying can be applied to reduce the cost of cold storage and also transit, means probiotic foods are sometimes dried to increase their shelf life by removing excess moisture at temperature and to decrease the cost of cold storage at very low temperatures −20 to −40 °C. Several drying methods can be applied however, freeze-drying, spray-drying, tunnel drying and vacuum-drying are the most well-known methods for bacterial culture preservation easily (Fonseca et al., 2015; Fu et al., 2018; Macro et al., 2019)

B. Biological factors

The Stability of probiotics are affected by biological factors like types of strain, antagonism with starter cultures, product natural microbiota, synthesized enzymes, post-acidification and presence of different pathogenic or spoilage causing microorganisms (de Melo Pereira et al., 2018). A favorable parameter for the choice of probiotic is to present functional, technical and safety measures, without giving negative features. The selected probiotic strain displays antagonistic features against various organisms resulting in damages of cell viability. Often the starter culture mainly used for food fermentation process influences the added probiotic culture (Hossain et al., 2017)
A particular reference regarding the production of fermented probiotic meat products as they are more complex than other probiotics-containing elements. The reasons related to raw material features (Kołożyn-Krajewska et al., 2012), viz high salt volume, lower pH and water activity for the acidification and drying processes (Terpou A. Papadaki et al., 2019). Health benefits like immune response pathways, strengthening of the epithelial barrier, and indirect impact on human pathogens can be confreres by proposed mechanism of probiotic (Marco.m. & Tachon 2013). The mechanisms are balancing activity through the gut brain axis (Bravo et al., 2011) and energy homeostasis (Chen et al., 2012)as well a function which may apply to probiotics conducts at other locations on the human body (Lemon et al., 2012)

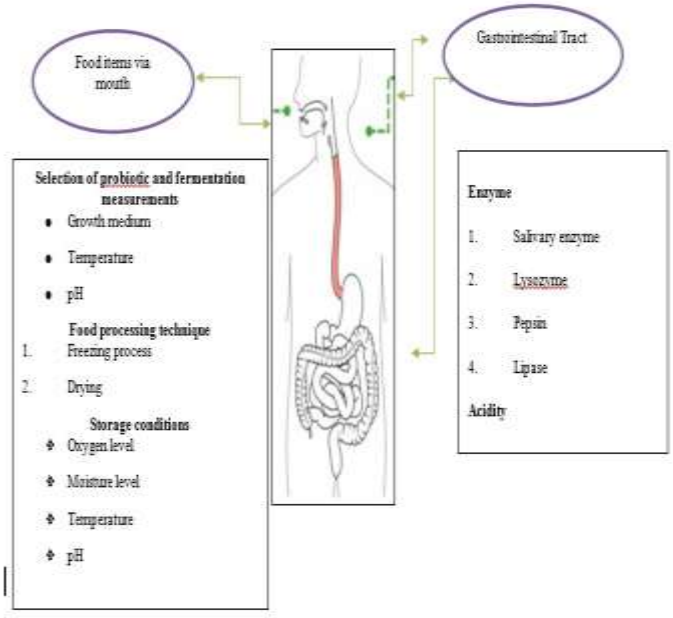

Fig 1: Factors affecting viability of probiotics in food product in Gastro Intestinal tract (Sornplang et al., 2016; Fuller 1992)

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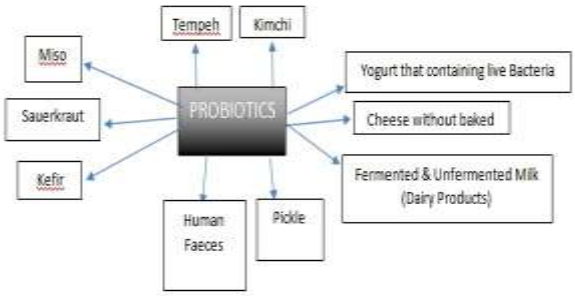

Fig 2: Different sources of probiotics (Sornplang et al., 2016; El-Mabrok et al., 2012)

IV. CHARACTERISTICS OF PROBIOTICS

A. The necessity of probiotics in intestine

The consequence of probiotics controls by their ability to stay passage through the stomach and duodenum and their ability to be temporarily present in, or to "settle", the intestinal lumen in intestine for an unspecified time period. When present, they may be capable to interact with both the host and the growing microbiota. In the two types of interactions, any probable health benefit will be controlled by the functional profile of the probiotics and on those sections in which they are present (Kerry et al., 2018)

When the host is human, interactions may be on a physiological, biochemical and/or immunological level. Some but not all, probiotic strains can decrease intestinal traverse time, enhance the quality of migrating motor complexes (usually forms contraction on muscle of the small intestine). The definition of a "normal" microbiota does not exist. It can be said that the probiotics are live microbes that is metabolically and functionally active. They are very beneficial for host, their metabolism has a neutral or deleterious effect on the microbes within the host microbiota (Ammor et al., 2008)

B. Translocation and infectious disease

In different papers the translocation of probiotic microorganisms has been listed in those people who are suffering from many diseases like cancer, AIDS, malnutrition. Probiotic microorganisms cause numerous nosocomial infections, they are-

Pneumonia- Lactobacilli are mainly very low virulence, mainly present in gastrointestinal tract. They are causing bronchiolitis with bacterial super infection. Lactobacillus pneumonia has been reported in immune suppressed patients with AIDS, after lung transplantation and after liver transplantation (Doern et al., 2014)

Liver abscess-Though it is very rare, liver abscesses can be related to L. acidophilus. There is reference to a single case in an immune compromised (by steroid treatment) patient with Crohn's diseases (Cukovic-Cavka et al., 2006)

Virulence factors-Toxicity regarding the probiotic strains under interpretation in this report, the ad hoc group got no reports of formation of particular toxins, deleterious to the body of host, by such strains.

V. ASPECTS OF PROBIOTIC METABOLIC FUNCTIONS

A. Degradation of mucin

A large amount of mucin is produced in the gastrointestinal tract by Goblet cells and enterocytes. The production of mucin parallels postnatal bacterial colonization and a wide array of bioactive factors that are able to stimulate mucin production have been described in the scientific literature. Mucin has many functions, and the most important one might be to act as a first line of defense for the underlying cells. Several antimicrobial peptides (defensins) are produced along the whole gastrointestinal tract and these peptides are retained by the surface-overlaying mucin, thereby providing a combined physical and antibacterial barrier against bacterial attachment and translocation. Under physiological conditions, gastrointestinal mucin is broken down by the indigenous microbiota, leaving little mucin to be excreted in faeces. It has been claimed, although never satisfactorily shown, that probiotics may regulate the balance between production and degradation of mucin. So, from above it can be concluded that reduced production or enhanced degradation of mucin may have path physiological effects, specifically in seriously ill patients. Administration of probiotics with these functions should be avoided in these patients. (Guarner et al., 2003; Meyer-Hoffert et al., 2008).

B. Antimicrobial Resistances

Probiotic strains belonging to Lactobacillus and Bifid bacterium may be resistant or susceptible to clinically-relevant antimicrobials. All Lactobacillus strains, but not all Bifid bacterium, are intrinsically resistant against vancomycin. In addition to this, a newly demonstration has been done to transfer van A gene from Enterococcus bacteria to a commercial strain of Lactobacillus acidophilus. The transformation occurred not only in vitro, but also in vivo in

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the gut of mice with no antimicrobial pressure (Lirussi et al., 2007). The transconjugants grow at comparatively high rate and could live in digestive environment. These studies confirm that horizontal gene transfer of antimicrobial resistance genes may occur in the gastrointestinal tract of animals and humans. This is of particular concern in hospital patients. Since long multi resistance found to be rare among Lactic acid bacteria and Bifidobacterial species while in specifically tetracycline and erythromycin resistance can be secluded (Lolis et al., 2008). There is a similarity between many of these gene determinants in bacteria of human origin and Lactic acid bacteria Bifidobacterium, which confirms that the spread of resistance genes between commensal microorganisms in the complex ecosystem does occur (Mater et al., 2008). In the past, many of the antimicrobial resistance genes in probiotic microorganisms such as Lactobacillus and Bifidobacterium strains were found to be located on the chromosome. Recently several antimicrobial resistant determinants in these microorganisms have been found to be located on plasmids and other mobile DNA-elements (Mater et al., 2005).

IV. MECHANISM OF PROBIOTIC ACTIVITY

A. Competition for adhesion receptors or sites

Probiotics fight for cellular attachments. The pathogenic organisms associate with the GIT epithelium to colonize themselves (Andrea et al., 2019). But due to presence of some strains of Bifidobacterial and Lactobacilli act as a "colonization barriers" by restricting the pathogens to club themselves with mucosa layer (Hemaiswarya et al., 2013; Borja et al., 2008; Andrea et al.,2019). As the species of Bifidobacterium and lactobacillus are most specific for probiotic bacteria usage, as both are gram-positive lactic-acid bacteria, both has same surface molecules which contains lipoteichoic acid and Surface Layer Associated Proteins (SLAPs) and mucin binding proteins (Mubs) which keeps a significant interaction with mucus components. The intestinal epithelial cells are much protected by glycocalyx layer which consists of glycolipids and glycoproteins, so due to this layer, it provides protection from mechanical damage and also protect the host bacteria by not allowing them to colonize with bacterial infections. So, this mucus layer consists of mucins, glycolipids, immunoglobins and electrolytes. Initially, bacterial interactions with intestinal layer can be by hydrophobic in nature and then can be by specific cell wall components (like Mubs, SLAPs). Researchers have executed that surface proteins like proteinases increase the adhesion to the intestine and hydrophobicity in Lactic acid bacteria.

Mucus binding proteins that are surface adhesion proteins are significantly found in lactic acid bacteria isolated from GIT of intestinal tract. So, this can bind effectively to mucins and link to peptidoglycan layer which help in adhesion of bacteria to intestinal mucosa layer. Hence, the presence of some bacteria in the intestinal tract is dependent on the ability to adhere to the gut epithelium, such that they become immobilized on the gut wall and resist being flushed out by peristalsis, as well as occupying a niche at the expense of potentially harmful organisms. (Miriam et al.,2012; Arthur et al.,2003)

B. Stimulation of immunity

Immune system is made up of two essential factors i.e., innate and adaptive immunity. They work in a combined way to protect us from external factors.

Studies with animal models have demonstrated strong immune responses, developed after probiotic bacteria interventions. Probiotic organisms interact with the epithelial mucosal layer of the host organism recruit the immune cells at the site of pathogenic infection and induce specific immune markers.

When L. casei was administered orally to mice and it has shown to activate the innate immunesystem via toll-Like receptors (TLR-2) cells which detects lipopolysaccharides and lipoteichoic cells in pathogens by which the immune system can trigger the immunological mechanisms like production of cytokinin (the toll-like receptors activate results in the initiation of dendritic cells which finally, helps in the production of cytokinin) (Ashraf and Shah, 2013).

The underlying mechanism of immune stimulation specially cell-wall components or cell layers may act as an adjuvant and increase humoral immune response (Hemaiswarya et al.,2013).

VII. WAY OF CONSUMING PROBIOTICS

- The microbe must be alive when taken, it must be documented to have a health benefit (Miriam et al.,2012; Mahasneh et al.,2010).
- These microorganisms will not provide benefits if they are not alive (Kavitha and Devasena, 2013).
- Manufacturers and customers should pay attention to storage conditions at which these microorganisms will survive (Seppo et al.,2021).

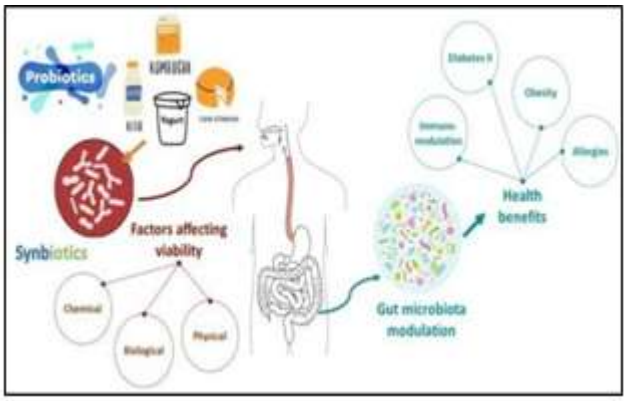

Fig 3: - Probiotics in Food System and their factors (Marco &Tachon, 2013)

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VIII. BENEFITS OF PROBIOTICS

- **Allergies:** Certain probiotics have an impact on the mucosal barrier function on the intestinal tract. This effects allergen entering the body and the activity of inflammation producing cells (Seppo et al.,2021).
- **Cholesterol:** Regular consumption of certain probiotic dairy products may have an impact on the cholesterol level and may affect the levels good HDL in the blood (Anadón et al.,2016).
- **Infant health:** Nature has long recognized the benefits of probiotics. Human breast milk contains mostly β casein which stimulates the production of MUC2 cells, MUC2 genes are most common mucin for the mucous layer and increase the number of goblet cells in the small intestine, which simply acts as a bodyguard for the further conversions and that stimulates the growth of good bacteria to help with digestion. Thus, a way to create and maintain a perfect balance of gut in babies has been in existence for as long as babies have been born (Pillai et al.,2020).

IX. SIDE EFFECTS OF PROBIOTICS

A. Digestive symptoms

The first use probiotics, some people experience gas, bloating, or diarrhoea. So, the changes in gut microbiota can result in the bacteria producing more gas than usual, leads to bloating (Zhang et al.,2020).

B. Infection

Use of various probiotics for immune compromised patients or patients with a leaky gut has resulted in infections and sepsis (infection of the bloodstream). One of bacteraemia (bacteria in the bloodstream) was recently found when someone with active severe inflammatory bowel diseases with mucosal disruption was given Lactobacillus sp.(Pace et al.,2020).

C. Histamine reactions

Histamines are chemicals formed by our immune system to fight against allergens. They insist our body to keep out allergens out of your system through allergic reactions like watery eyes, stuffy noses, minor rashes, and itchy skin.

Most probiotic supplements consist of a combination of histamine producing, histamine neutral, and histamine reducing bacteria, so they typically do not have a strong effect on overall histamine levels in the body.

So, allergic reactions are still a possibility in histamine sensitive individuals. If common allergic reactions take place after taking probiotics, it could signify an overload of histamine or gut bacteria imbalance (Ö Özdemir 2010)

D. Future perspectives of probiotics

Present development in technology & methodology offers dramatic possibilities for Probiotics research and applications. New tools providing real time studies in man and following microbes as it unifies into an existing microbiota as well as can enhance levels of health, will take this field ahead.

Studies of present microbes, their synergy with the host & the effect of environmental factors (e.g., drugs, nutrients) will become standard when approaching for physical examination in the future.

Novel sampling system will interpret how these probiotics interact with host at different levels including the immune System, metabolism & all components of the microbiome. Finally, a unified approach will provide a form of personalized medicine to ease set up dose-response relationships for treatment and will provide alignment of what enters our body, how it is processed and which probiotic can provide best effects. And the mechanistic insights into effector molecules will lead to new emerging concepts like probiotics.

XI. CONCLUSION

In conclusion, this report describes the overview of probiotics, when humans are affected by any infection there are more bad bacteria than good one's so there's an imbalance in our body. When good bacteria are inserted in our body, eliminates extra bad bacteria giving a balance to our body. Most of beneficial microbes live in our large intestine (gut). Probiotics were found to effectively influence the host by enhancing their microbial balance of intestine, thus suppressing pathogens and toxin forming bacteria. Lactobacillus, Bifidobacterium are two specific types of bacteria found in probiotics. Probiotics can also be made up of yeasts like Saccharomyces boulardii. The increase in the number of beneficial microbes from foods (yoghurt, sourdough bread, cottage cheese, tempeh, fermented pickles etc.) to strengthen our microbiome. Probiotics helps humans to take out from various problems like diarrhoea, constipation, irritable bowel syndrome, urinary tract infections, sepsis, lactose intolerance and many more. Probiotic supplements can be taken in form of drinks, capsules, powders which should be recommended by Federal drug administration (FDA) for safety and effectiveness. Probiotics are safe in most conditions but there may arise some risks in supplements, if any recent surgery undergone causing to any infection, resistance to antibiotics and developing any harmful by products from probiotic supplement. So, it has to be kept in mind that not all probiotics have same function rather different in their own aspects and has their own benefits, but they do not cause harm, generally.

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