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A Review; Probiotic

Kothawade Priti [1*], Layare Aparna [2], Shinde Anushka [3], Dr.M.R.N.Shaikh [4]

1- Assistant professor, (Department of pharmacology) MET Institute of D.pharmacy, Nashik-422003

2 and 3 –MET Institute of D. pharmacy, Nashik-422003

4-Principal of MET Institute of D.Pharmacy, Nashik-422003,Maharshtra Nashik

Abstract

Probiotics are commonly defined as viable microorganisms (bacteria or yeasts) that exhibit a beneficial effect on the health of the host when they are ingested. Numerous scientific studies have demonstrated their advantages for both human and animal health. The two primary probiotic groups are Lactobacillus and Bifidobacterium; however, there have been findings on the probiotic potential of yeasts, Pediococcus, Lactococcus, and Bacillus. Probiotic strains that have been found possess significant anti-inflammatory and antiallergic characteristics, among other key attributes. Aside from that, eating both dairy and non-dairy products boosts immunity in various ways. Probiotics have been employed with a variety of dietary matrices; a brief history is provided. This overview covers the history of probiotics, their use in food and health, and the latest developments in probiotic procedures and products.

Keywords-Probiotics, History, Classification, Mechansim, Application

Introduction

According to the FAO (Food and Agriculture Organisation of the United Nation) and WHO (World Health Organisation), probiotics are: "Live microorganisms that, when administered in sufficient quantities, benefit the host's health."
Probiotic bacteria are now increasingly used in the nutrition manufacturing and in commercial products like dietary supplements due to their positive impact on immune function, growth performance and in the treatment of many diseases and disorders like GIT and respiratory disorders etc.

In addition to the use in human foods, probiotics are also used in animal foods to strengthen and stabilize animal growth and products.For a functional probiotic with a suitable daily dosage of 10^6-10^9 living bacteria, the count of living microorganisms should be greater than 6 log cfu/g in order for probiotics to be effective for humans.

Various species of *Bacillus* genus have been found effective for application in food and agricultural industries. The spores of various *Bacillus* species, including *Bacillus subtilis*, *Bacillus cereus*, *Bacillus clausii*, and *Bacillus coagulans*, are used to produce probiotics. *Bacilli* bacteria, which are ubiquitous in food, water, and air, can enter the gastrointestinal tracts of humans exposed to these sourcesDue to spore forming, there is a huge advantage in the strain survival during pellet formation and they also possess pathogen exclusion, antioxidant, antimicrobial, immunomodulatory and food fermentation abilitySince the human gut contains 10^7 cfu or more of *Bacillus* species, they are thought to be one of the dominant elements of the normal gut microflora.

1. Probiotics:

'Probiotics'arelivemicroorganismswhichwhenadministeredinadequateamountsconferahealthbenefit onthehost.'ThetermprobioticwasderivedfromtheGreekword"forlife''. FAO(FoodandAgriculture Organization)andWHO(WorldHealthOrganization)havestatedthatthereisadequatescientificevidence toindicatethatthereispotentialforprobioticfoodstoprovidehealthbenefitsandthatspecificstrainsfor safe human use. Probiotics were originally used to improve the health of humans and animal through the modulation of the intestinal microbiota, stimulation and development of the immune system. The main effectofprobioticsattheintestinallevelsuchasbalancingandrestorationofthegutmicrobiota,protection against pathogens, immunomodulation, and maintenance of intestinal barrier integrity.
Thetermprobiotictakenasunchallengedsynonymforbeneficialmicrobeshasgainedpopularly overthe years and has found application in several general health and clinical scenarios. Probiotics found applications with various health benefits in human and animal feed for the prevention of gastrointestinal infections with extensive use in poultry and aquaculture industries· The emergence of cross-resistance in pathogenicbacterial strains has ledto thebanning ofantibiotic growth promoters(AGPs). Therefore, the need for alternative approaches is increasing and 'probiotics' has been proved to be one of the best alternatives.Asprobioticmanymicrobeshavebeenusedcommercially,like*lactobacillus*species,*bacillus* species,*enterococcus*species,and*Saccharomyces*species.*Lactobacillus*and*Bifidobacterium*arethemost widely or commonly used bacterial probiotics. Various species of the *Bacillus* genus have been found effective. Due to spore-forming, there is a huge advantage in strain survival during pellet formation. Endospores former such as bacillus species are interesting because their spores resist the acid barrier of the stomach and are stable for long periods in commercial food products·*Bacilli* considered gut commensal have been used as probiotics for prophylaxis of human gastrointestinal disorders

1.1 HistoryofProbiotics:

Thetermprobioticisarelativelynewwordmeaning"forlife"anditiscurrentlyusedtonamebacteriaassociated with beneficial effects for humans and animals. The original observation of the positive role played by some selectedbacteriaisattributedtovariousscientists.Theconceptofprobioticswasthusbornandanewfield of microbiologywasopened

Table.1: History ofprobiotics:Variousscientists andtheirstatements

Sr.no	**Scientists/Year**	**Statement**
1.	Elie Metchnikoff (1908)	Suggested that rod-shaped bacteria found in fermented dairy products (*lactobacillus spp*.) offer health benefits. As a result, these bacteria have a beneficial effect on the gut microbiota and lessen the harmful activity of microorganisms in intestine.
2.	Greek and Romans (1925)	Thehistoryofprobioticsbeganwiththeconsumptionof fermented diets

3.	American Academy PediatricCommitteeon Nutrition (1980)	Probiotics are microorganism that generates small molecular metabolic by-products that made beneficialregulatoryeffectsonhostbiological functionandmayfunctionasimmunomodulators
4.	Lilly and Stillwell (1965)	'Substancessecretedbyonemicroorganismthat stimulate the growth of another'.
5.	Parker(1974)	ProposedthatProbioticsare'organismsandsubstances whichcontributetointestinalmicrobial balance'.
6.	Fuller(1989)	Heredefinedthewordas"dietarysupplementoflive microbesthatbeneficiallyaffectthehostbyimprovingits intestinal balance".
7.	HavenerandHuisIntVeld (1992)	Redefined probiotics as "live cultures, consisting of one or more microbes which, when administered to animals or humans,arebeneficiallyaffecting thehostbyimproving the propertiesoftheintestinal flora".
8.	GuarnerandShaafsma(1998)	Definedas"live microorganisms, whichwhenconsumedin sufficient quantities, produce beneficial effects on the host beyond those of basic nutrition".
9.	ILSI(InternationalLife Sciences Institute) Europe (1986)	Defineditas"Alivemicrobialfoodingredientthatisbeneficial to health"
10.	Schrezenmeit and de Vrese (2001)	Defined "Probiotics are a preparation of microorganisms or a product that contains live, defined microorganisms, which positively alter the composition of the microflora by implantation or colonization in a host's residence, after repeated periodical reintroduction, thus exerting beneficial effects on health"
11.	Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO, 2001)	Defined Probiotics as "Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host"

1.2 Microorganismsusedasprobiotics/Classification:

The microbes usedas Probiotics represent different types suchas yeast, bacteria, or mold. However, there aremore common species of each such as

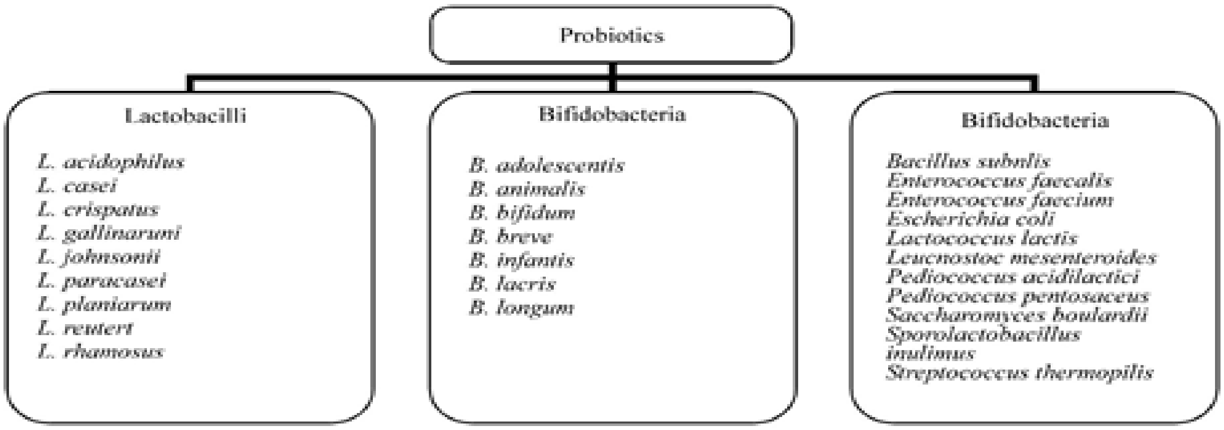


Fig 1 : Classification of probiotics

1.2.1 -Bacteria

(i) Lactobacillus:*Plantarum,rhamnosus,acidophilusdelbrueckii,reuteri,brevis,casei,paracasei,gasseri, crispatus.*

(ii) Bifidobacterium:bifidum,infantis,adolescentis, longum,breve,lactis, animalis.

(iii) Streptococcus:lactis,cremoris,alivarius,intermedius,thermophilis,diacetylactis.

(iv) Leuconostocmesenteroide

(v) Pediococcus.

(vi) Propionibacterium.

(vii) Bacillus.

(viii) Enterococcus.

(ix) Enterococcusfaecium.

1.2.1.1 -*Lactobacillus*

Lactobacilli are gram-positive, non-spore-forming rods that are frequently found in the mouth, GI tract, and female genitourinary tract. They are an essential component of the normal human bacterial flora. Microscopically , these bacteria resemble thin, non-motile rods that range in length from long to small.except in cases when they are linked to dental caries, *lactobacilli* are not often regarded as pathogens in healthy hosts because they are necessary to maintain a healthy GI tract.These organisms are regarded as "protectory" and may inhibit pathogenic growth by producing lactic acid and other metabolites.One of those features is the ability to produce bacteriocins(Small proteins called bacteriocins are made by bacteria and can be harmful to other bacteria), which are low-molecular-weight antimicrobials.

1.2.1.2-Bifidobacterium

Bifidobacteria were first isolated and described in 1899-1900 by Tissier, who characterize rod- shaped, non- gas producing, anaerobic with bifid morphology, present in the faeces of breastfed infants, which he term bacillus bifidus.The general characteristics of *bifidobacteria* are that they arecatalase-negative, gram-positive, non-spore-forming, non-motile anaerobes. The gut microbiome has been extensively studied using *Bifidobacterium* as a probiotic, with the aim of altering its composition to reduce diseases. Additionally, bacteria can be used in culture or colony development. *Bifidobacterium*, similar to other *lactobacilli*, can inhibit harmful bacteria, enhance gastrointestinal barrier function, and suppress pro-inflammatory cytokines.

Recent studies have shown that *Bifidobacterium* alter dendritic cell function to control intestinal immune homeos tasis against antigens and harmless bacteria or to initiate defense mechanisms against pathogens.Thecombination of *Lactobacillus* and *Bifidobacterium* reduces stress and depression.

1.2.1.3-Others :

Enterococcus :

Enterococcus are gram-positive bacteria in the lactic acid bacteria family.the Gram-positive *cocci* that were formerly classified as *streptococci* were reclassified as *streptococcus*, *lactococcus*, and *enterococcus*.The new genus *Enterococci* contains the *faecal streptococci* that are present in the gastrointestinal tracts of both humans and animals as well as in a variety of different environments. Certain *Enterococcus* strains have immune system-modulating properties, exhibit antibiotic-induced dysbiosis, and have antitumor or anticancer properties.The culture of an E. faecium strain from human intestinal epithelium has been found to boost the bactericidal activities against enteroaggregative *E. coli*, membrane damage, and cell lysis.

1.2.2- Yeastand moulds:

Saccharomyces cerevisiae, Saccharomyces bourlardii, *Aspergillus niger*, *Saccharomyces boulardii*.The type of microbes used as Probiotics increased due to the increase in the research concerning the subject as well as bytheincreaseofthenewlydiscoveredandidentifiedmicrobes,whichcouldbeusedasProbiotics.Following are the requirements which have been identified for a microorganism to be defined as an effective probiotic**:**

- Theprobioticshouldgivepositiveeffects onGIT ofthehost.It shouldbeacidresistant,bileresistant.
- Theadhesivecapabilityof probioticsmustbefirm and faster.
- Theprobiotic shouldpossess highsurvival rate&multiply faster.
- Excludeorreducepathogenic adherence.
- Safe,noninvasive,non-carcinogenic,andnonpathogenictothehostProduceacids,peroxideand bacteriocins, antagonistic for the growth of pathogens.
- Coaggregationtoformanormalbalancedflora.
- Probioticsshouldbedurableenoughtowithstandtheduressofcommercialmanufacturing,processing, packing and distribution so it can be delivered alive to the intestine.

1.2.2.1-Saccharomyces

A selective probiotic yeast that is non-pathogenic and used in the production of probiotic food **.**A number of studies have demonstrated that *S. cerevisiae* and *S. boulardii* were associated with an increased proportion of Bacteroidetes in the gut microbiota composition and a reduced relative abundance of Firmicutes and Proteobacteria. Furthermore, this yeast can reduce inflammation by boosting proinflammatory immune responses and short-chain fatty acid synthesis.

1.3 Sourcesofprobiotics

Theprobioticbacteriaoftencomefromthegenera*Lactobacillus*and*Bifidobacterium*.However,someyeastand other bacteria also possess probiotic qualities The most common source of probiotics is Yogurt. Yogurt consists of milk (usually from the cow, goat or sheep) fermented by bacteria that modify lactose into lactic acid. Lactic acid is responsible for giving yogurt its characteristics (sharp taste usually changed into good taste by using sweetenersandflavouringagent)andalsodenaturesandprecipitatescasein,resultinginasemisolidconsistency. ‘‘Bioyoghurtsareproducedinasimilarway,butbacteriausedforfermentationareofdifferentstrains,usually *L.acidophilus*.Fermentedmilkandfortifiedfruitjuicearecommonsourcesofprobiotics.

1.4 SelectionCriteriaforProbiotics

Before a probiotic can be useful in the interest of human health, it must have several criteria: it should have the desired technological properties so that it can be produced and added to the food products without losing its survival and function, or creating an unpleasant taste or tissue; it must survive when passing through the gastrointestinaltractandmustreachlivesiteandshouldbeabletofunctionintheintestinalenvironmentSeveral aspects should be considered in the selection of appropriate probiotic

1) Safestrains, species, andgeneraof probiotics
2) Viabilityandbioactivityduringtheprocessand storage
3) Gastrointestinalsurvival and resistanceto gastricacidand bileacids.
4) Stimulating the selection of beneficial bacteria and suppressing harmful bacteria (through the production ofantimicrobial compounds and competitive elimination)
5) Antagonisticactivityagainstpathogenssuchas*Helicobacterpylori*,*Salmonella*,*ListeriamonocytopeniaClostridium difficile*.
6) Adhesiontotheintestinal epithelium
7) Anti-mutagenicandanti-carcinogenicproperties Modificationand improvement ofthe immunesystem

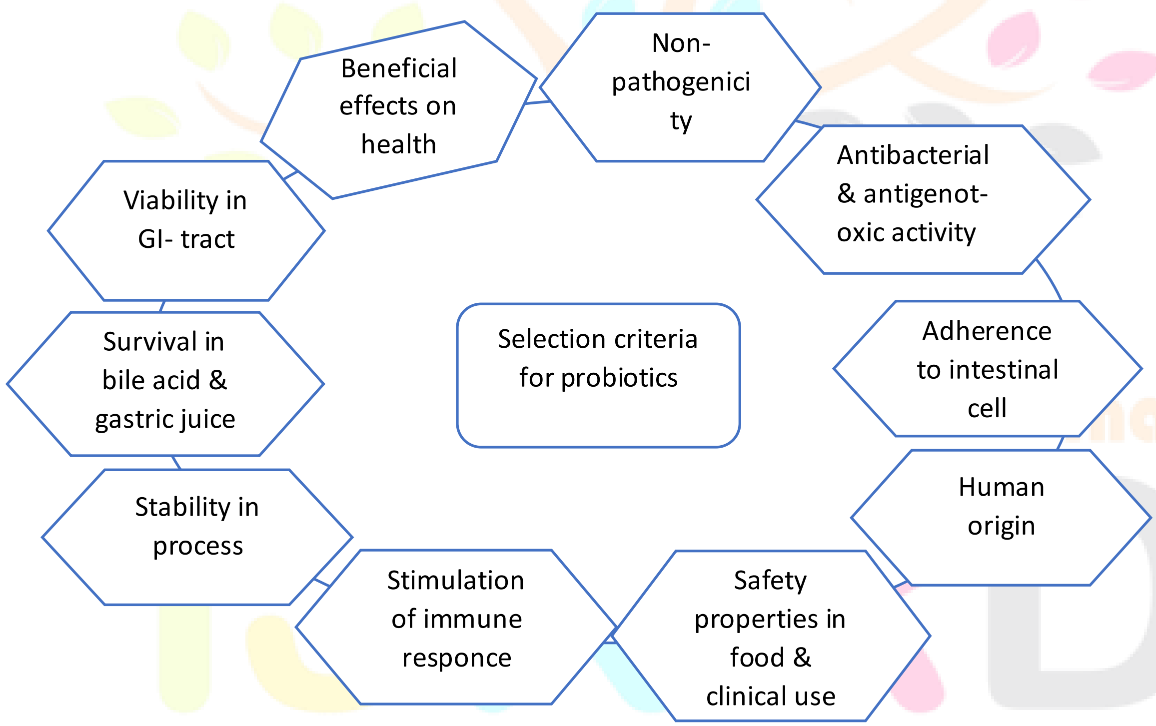


Fig.2: Selectioncriteriafor Probiotics

1.5 Role and properties of probiotics:

Probioticsplay amajorrolein thetreatment andprevention ofmany diseasesand disorders.

- RoleofProbioticsinPreventing Diarrhoea
- RoleofProbioticsinLactose Intolerance
- RoleofProbioticsin ControlofGastro-Intestinal Tract
- RoleofProbiotics asaFunctional Food
- RoleofProbiotics in Cancer

- RoleofProbiotics as Anti-Oxidants
- RoleofProbioticsin Hypercholesteremia
- RoleofProbiotics inBacterialVaginosis
- RoleofProbiotics inDiabeticActivity

Fig.3:PropertiesofanidealProbiotics

Various studies have indicated that Probiotics may alleviate lactose intolerance; have a positive influence on the intestinalfloraofthehost;stimulate/modulatemucosalimmunity,reduceinflammatoryorallergicreactions reducebloodcholesterol.possessanti-coloncancereffects,reducetheclinicalmanifestationsofatopicdermatitis, Crohn's disease, diarrhoea, constipation, candidiasis, and urinary tract infections ,and competitively exclude pathogens Considering this impressive list of potential health-promoting benefits, it is not surprising that there continues to be considerable interest in the use of probiotics as biotherapeutic agents .Furthermore, given a heightenedawarenessamongconsumersofthelinkbetweendietandhealthandthefactthatProbiotics-containing foods are generally perceived as "safe" and "natural," the global market for such foods is on the increase, particularly dairy- based products marketed for the prophylaxis or alleviation of gastrointestinal disorders.

1.6 Ideal Propertiesof probiotics

- It should be capable of surviving and metabolizing in gut environment e.g., resistance to low PH and acids.
- It should be strain specific exerting beneficial effect on host animal. It should be present as viable cells, preferably in large numbers and it is acid and biletolerant (ability of bacteria to survive in stomach and small intestine).

HealthBenefits	Proposedmechanism involved

Resistancetoenteric pathogens	Antagonism activity, Adjuvant effect increasing, antibody production, Systemic immune effect, Colonization resistance Limiting access of enteric pathogens(pH,bacteriocins/defensins,antimicrobialpeptides, lacticacidproduction, andtoxicoxygen metabolites)
Aidinlactosedigestionsmallbowel bacterial overgrowth	Bacteriallactaseactsonlactoseinthesmall intestine- Lactobacilli influence the activity of overgrowth flora, decreasing toxic metabolite production Normalizationofasmall bowelmicrobialcommunity Antibacterialcharacteristics
Immunesystem modulation	Strengthening of nonspecific and antigen-specific defense against infection and tumours Adjuvanteffectinantigen-specificimmuneresponses Regulating/influencing Th 1/Th2 cells, productionofanti-inflammatorycytokines
Urogenitalinfection	Adhesiontourinaryandvaginaltractcells Competitive exclusion Inhibitorproduction(H2O2,biosurfactants)
InfectioncausedbyHelicobacter pylori	Competitive Colonization Inhibitionofgrowthandadhesiontomucosalcells,decreasein gastric H.pylori concentration
Hepatic encephalopathy neutralization of dietary carcinogens	Competitiveexclusionorinhibition ofureaseproducinggut flora Productionofbutyricacidneutralizestheactivityofdietary carcinogens
NEC (necrotic inflammation of the distal small intestine)	DecreaseinTLRsandsignallingmoleculesandincreasein negative regulations ReductionintheIL-8response
Rotaviral gastroenteritis	Increased IgAresponsetothe virus
Inflammatory bowel disease, type I diabetes	Enhancementofmucosalbarrierfunction
Crohn'sdisease	Reduction in Proinflammatory cytokines including TNFα, reductioninthenumberofCD4cellsaswellasTNFαexpression amongintraepitheliallymphocytes

- Itshouldberobustandsurvivingprocessingconditions.
- Itshouldbegeneticallystableunderstorageand field conditions

1.7 Health benefits of probiotics

Itshouldbenon-pathogenicandnon-toxic It is now an established fact that the indigenous microbial communities is host specific, location specific, very complexincompositionandhasbeneficialpropertiestothehost.However,itisnotpreciselyknownwhichspecies ofmicroorganismsplaytheprincipalpartinthesebeneficialproperties.Somemajorhealthbenefitsofprobiotics and their proposed mechanisms are illustrated in Table no.2

Table.2:Healthbenefitsofprobioticsandtheirmechanisms

TheprimaryclinicalinterestintheModulationofanunbalancedindigenousmicrobiotaservesasthebasis forprobiotictherapybecausevariationsinthegutmicrobiotahavebeenlinkedtoincreasedriskofcertain diseases. Additionally, due to the rapid emergence of antibiotic-resistant pathogenic strains and the negative effects of antibiotic therapies on the protective flora, which increases the risk of infection, the developmentofadjuvantoralternativetherapiesbasedonbacterialreplacementisbecomingincreasingly important. Probiotic use should be further researched to determine any potential benefits and negative effects. As our understanding of the relationship between diet, immunity, and genetics in health and diseasehasgrownoverthepastfewyears,thisknowledgecoulddefinitelyaidinthedevelopmentofnew probiotic strains with disease-specific functions. the application of probiotics has been in the prevention and treatment of GIinfections and diseases. However, it is important that theprobioticstrains for human useshouldundergoanimalstudiesfollowedbyhumanclinicaltrialsinordertoauthenticatethesuitability, safety, and benefits of probiotics for human consumption and the development of functional foods.

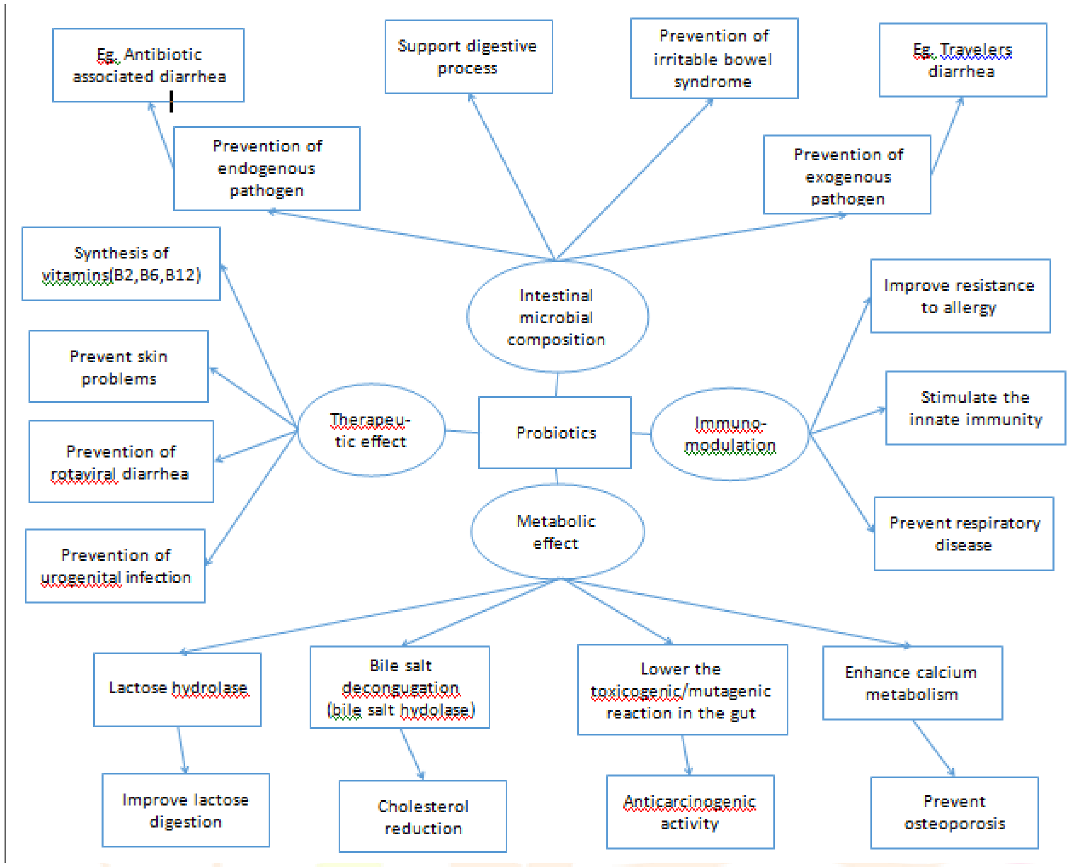
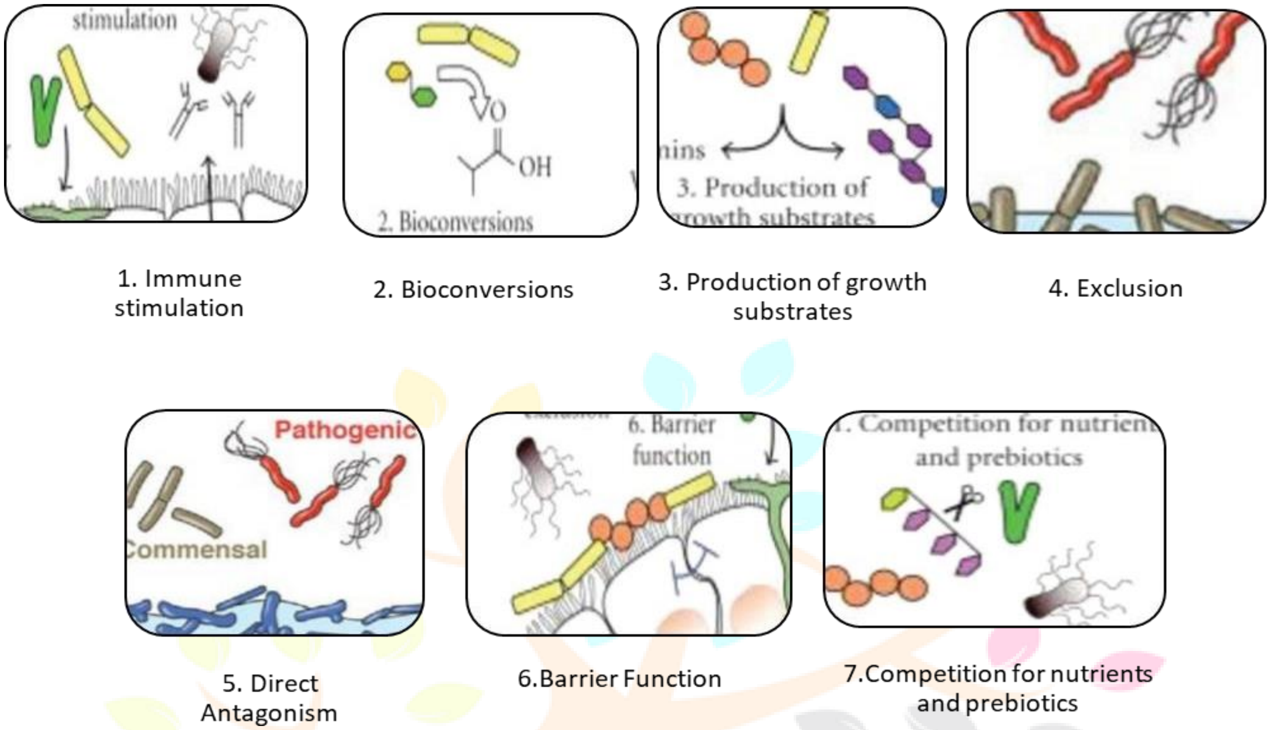


Fig.4: HealthBenefitsof Probiotics

Probioticsalsoplaymajorroleinreducingserumcholesterollevels,ProbioticsplayamajorroleinLactose intolerance, Diarrhoea, Anti-carcinogenic properties, Enhances Immune system, Atopic Dermatitis, Urinary tract infections .

1.8 Mechanism ofProbiotics:

The main mechanism by which probiotics play a beneficial role in animals is described as (i) production of antibiotic substance, (ii) compete with harmful bacteria for nutrients, (iii) adhesion and colonization in the intestinal mucosa, (iv) reducing the stress response and enhancing the immunity, and (v) regulating the binding



of cytokines to receptors to regulate the immune response.Theexactmechanismbywhichprobioticscarryouttheirbeneficialimpactsisnotwellunderstood.

Fig.5: VariousMechanisms ofprobiotics

One such mechanism involves probiotics competing for cellular attachments by competing for adhesion sites. To successfully colonize, a variety of pathogenic organisms must collaborate with the gastrointestinal endothelium. However, some *bifidobacterial* and *lactobacilli* strains can hold fast to the epitheliumandserveas"colonizationbarriers"bypreventingpathogensfromstickingtothemucosa,this is not always the situation.The modification of the microbial flora through the synthesis of antimicrobial compoundsisanotherpotentialmechanismofaction.Bacteriocinsandotherantimicrobialsubstancesare producedbyawidevarietyoflactobacilliandbifidobacterial."Compoundsproducedbybacteriathathave a biologically active protein moiety and a bactericidal action" are referred to as bacteriocins. The lactic acid bacteria also produce short-chain fatty acids, hydrogen peroxide, and diacetyl, all of which are biologically active substances. Probiotic organisms release these chemicals, which alter the microflora positivelyHowever,notallstrainsoflactobacilliorbifidobacterialproduceantimicrobialsubstances,and some produce substances with relatively nonspecific activities, which might harm both pathogenic and beneficial bacteria.

1.8.1 EnhancementoftheEpithelial Barrier:

Theintestinalbarrierisacrucialbarriersystemthatkeepstheepitheliumintactandprotectstheorganism from its surroundings. The antimicrobials mucous layer, secretory IgA, and the epithelial cells that form tight connections make up the intestinal barrier's defenses. A number of clinical disorders, including bowel illness, liver disease, and GIT infection, have been associated with epithelial barrier disruption. Importantly, consuming probiotic bacteria can improve intestinal barrier performance. The enterocytescreate thick mucus that is released by mucus and distributed throughout the luminal epithelium of the intestines, enhancing the epithelial barrier.probiotic bacteria havebeen shown to stimulateintestinal epithelium inflammation, which in turn increases mucus output.

Numerous studies have suggested that enhancing the expression of genes related to tight junction signaling is a potentialmethodformaintainingthefunctionoftheintestinalbarrier. Thetightjunction signalingpathway can be induced by certain probiotics. For instance, in a T84 cell, lactobacilli alter the regulationof E-cadherin and -catenin. Ingastrointestinal disorderslike IBD,changesin pro-inflammatory cytokine levels can cause intestinal permeability. By preventing the production of cytokines, probiotic bacteria consumption reduces cytokine-induced epithelium damage (TNF).

1.8.2 IncreasedAdhesion toIntestinal:

Since probiotic bacteria can attach to epithelial cells, they can prevent pathogen adherence. Probiotics may induce the production of mucin, a complex glycoprotein mixture that is a component of mucous, which inhibits the adhesion of pathogenic bacteria, or they may compete with pathogens for the same receptorasaresultoftheiranti-adhesiveeffect.Accordingtoseveralstudies,various*lactobacilli*proteins promote mucous adhesions and bacterial surface adhesions serve as a pathway for attachment to the mucous layer.

1.8.3 Competitiveexclusion ofpathogenicmicroorganisms:

Exogenous pathogens are competitively prevented from the environment by local bacteria due to competition for adhesion space. *E. coli, Salmonella, Helicobacter pylori, Listeria monocytogenes*, and Rotavirusarejustafewofthepathogensthat*lactobacilliandbifidobacterial*havebeenshownto inhibitProbiotics' ability to physically block pathogenic bacteria from colonizingtheir preferred sites, such as the intestinal cell, epithelium, and colonic crypts is one of the many mechanisms and characteristics that probiotics use to inhibit pathogenic adhesion.

1.8.4 Productionofanti-microbialsubstances

Probiotics can produce antimicrobial substances that can prevent pathogen replication. Short chain fatty acids(SCFA),antimicrobialpeptides(AMPs),organicacids,anddeconjugatedbileacidsareexamplesof LMW compounds that are almost always present in these components. This LMW group contains short- chain fatty acids, which is significant. Acetate, propionate, and butyrate are among the short-chain fatty acids (SCFA) that are created by intestinal bacteria during the fermentation of dietary plant material's insoluble fiber. Acetic acid and lactic acid in particular, which have a potent inhibitory effect against Gram-negative bacteria, have been thought to be the main antimicrobial compounds causing probiotics' inhibitory activity against pathogens.

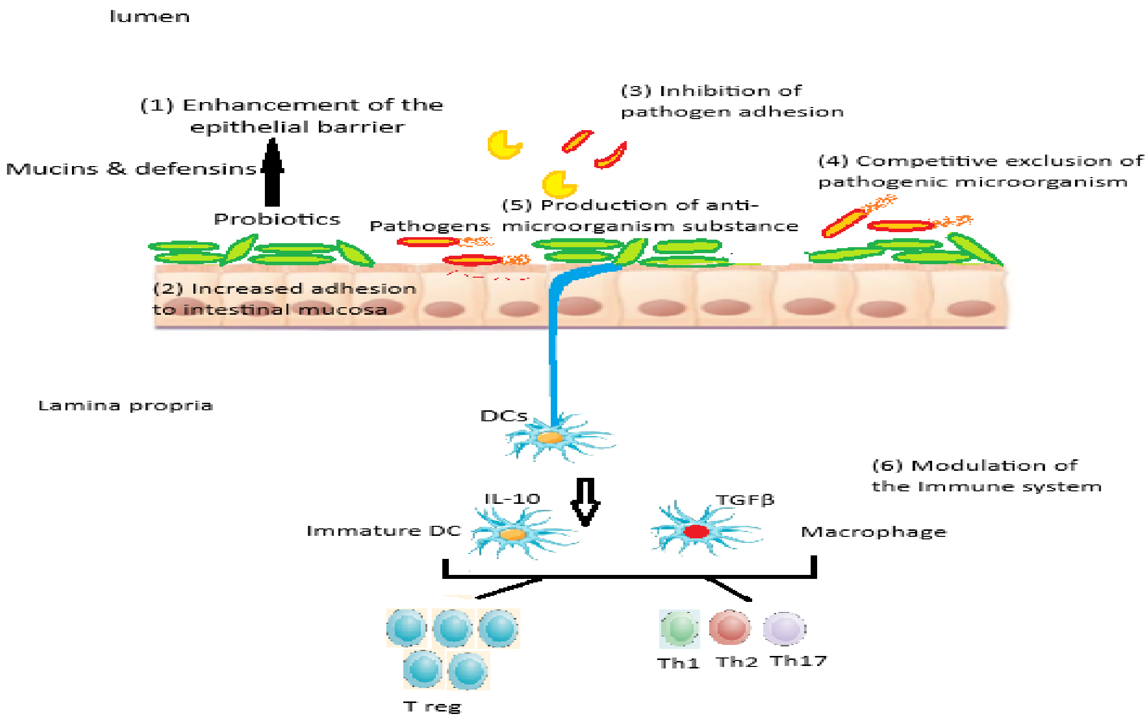


Fig.6:MechanismofProbiotics

1.9 Probiotics and their immune system:

Numerous cell types involved in adaptive and innate immune responses, including epithelial cells, dendriticcells,monocytes/macrophages,Bcells,Tcells,regulatoryTcells,andNKcells,canbeaffected byprobioticbacteria,whichthenexerttheirimmunomodulatoryeffect.ProbioticbacteriacanlowertheT lymphocyteresponseandpreventdendriticcellsfromproducingtheproductionofcytokinesIL-12,TNF, and IFN (DC). Children with the gastrointestinal disease who were given L. rhamnosus GG noticed an increaseinnon-specific-specifichumoralimmuneresponsesviacirculatinglymphocytessecretingthe most IgG, IgA, and IgM One such mechanism involves probiotics competing for cellular attachments by competingforadhesionsites.Tosuccessfullycolonize,avarietyofpathogenicorganismsmustcollaborate.
the Gastrointestinal endothelium. However, some *bifidobacterial* and *lactobacilli* strains can hold fast to theepitheliumandserveas"colonization barriers" bypreventingpathogens fromstickingto the mucosa, thisisnotalwaysthesituation.The*Lactobacilluslactobacillusacidophilus*strainGGandthe*Lactobacillus Plantarum*299vwereusedtodemonstratethiseffect.Bothoftheseorganismsdemonstratedtheabilityto preventEscherichia colifrom strictadherencetohumancoloncells.Other proposedmechanismsforhow intestinal microflora is affected include lowering intestinal pH, releasing gut-protective metabolites, controlling intestinal motility, and producing mucus. The primary point of contact between the immune system and the outside world is the mucosa of the gastrointestinal tract. Antigen transport increases whenever intestinal microflora decreases, indicating that the healthy gut microflora maintains gut defenses. To initiate the immune signals, the non-pathogenic probiotic bacteria interact with the gut epithelial cells and the immune cells. These bacteria must interact with gut epithelial cells, associated immunecells, and M cells in Peyer'spatches. The production of immunoglobulins has been shown to be modulated by probiotic bacteria. Mucosal immunity benefits from secretory IgA, which helps to form a defense against pathogenicbacteria and viruse.

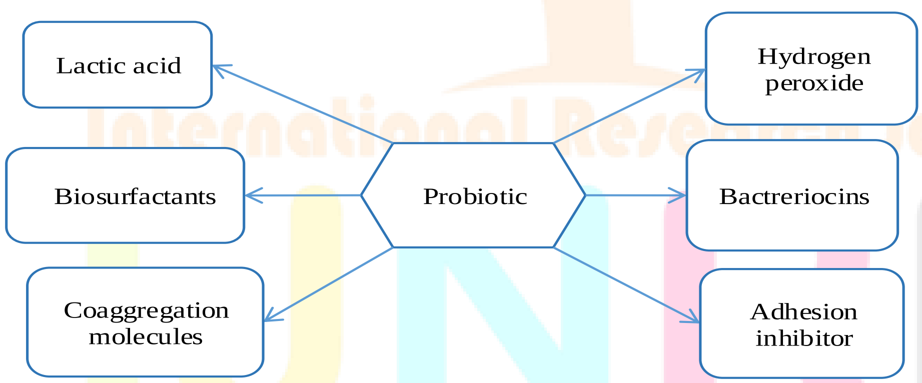


Fig.7: Metabolic products ofProbiotic

Themost remarkable characterof probioticorganisms was the increase in IgA-producing cells, though it hasalsobeenshownthatfermentedmilkyogurtcanalsoinduceIgAindependently.Thestimulationwith probiotic bacteria has also been observed to increase the profiles of some cytokines (TNF- IFN-, IL-10). Inordertoup ordown-regulateimmuneresponsesandpreserveintestinalhomeostasis,thereleaseof cytokinesisinduced.ItisstillunclearhowprobioticmicroorganismsinteractwithGALT(Gut-associated lymphoid tissue), as well as how they exert their anti-inflammatory and immunomodulatory effects.

1.10 Safetyof Probiotics:

This study's objective was to assess the safety of products that contained probiotic strains. According to observations, these products are increasingly helping people with immunosuppressed systems or vulnerable individuals,suchastheelderly,children,andthosewithimmunedeficiencies.Suchanideologyleadstoconcerns aboutprobiotics'safety.Theprobioticstrainsshouldnotharmthehostandshouldbecompletelynon-pathogenic. It is difficult to find evidence to back up this assertion.

TheProbioticSafety Assessmentstudies useavariety oftechniques, including

1. Studytheparticularcharacteristicsofdifferent probioticstrains
2. Investigationintotheprobioticstrains'pharmacokineticandpharmacodynamic
3. Researchintohowprobioticsandhosts interact.

Themosteffectivewaytoevaluatethesafetyofanewprobioticinanimmunocompromisedhostisonlythrough theanimalmodel.Thesafetyofaprobioticfoodproductisdefinedastheabsenceofanysignificantadversehealth effectsfollowingconsumptionunderspecificcircumstances.Duetotheirextensivehistoryofsafeuse,probiotics are effective. *Bacillus* species, a probiotic, is widely distributed throughout the environment and can be isolated from water, soil, air, and decomposing plant matter, most likely as a result of indirectly consuming plant matter. SomeBacillusspeciesbacteriahavealsobeenfoundinthegastrointestinaltractofanimals.Animportantsource of enzymes for food, animal feed, and numerous industrial uses are the *Bacillus* species. In Asia, a number of exclusive *Bacillus* probiotic strains have been marketed as dietary supplements. *Bacillus* probiotics' mechanism is still poorly understood. The following traits are probiotic safety dimensions.

1. Humanorigin should bepreferred forprobioticstrains intended forhuman consumption.
2. Theyneed tobe maintainedapart fromahealthyhuman digestivesystem.
3. Theyshouldn'thavea backgroundthat makesthem pathogenic.
4. Theyshouldn'tbeconnectedtoconditionslike infectiousendocarditisordigestiveissues.
5. Theyshouldn'thydroxylate orreducecongestionof bilesaltsin thesmall intestine.
6. Theyshouldn't havegenes that makethem susceptibleto antibiotic resistance.

Probiotics are assumed to have beneficial benefits, produce antimicrobials, stimulate the immune system, and improve gut flora. Through a series of in vitro, in vivo, and clinical studies, the safety of probiotics *Bacillus coagulans*and*B.subtilis*intendedforconsumptionbyhumanswasevaluated.Variousresearchersevaluatedthe safetyofprobiotics,butthefullimplicationsofthesafetydatawerenot reported.

1.11 DIFFICULTIES IN RECOGNIZING PROBIOTIC INFECTIONS

Due to the anaerobic nature of probiotic bacteria, it has always been difficult to demonstrate that they are infectious .Additionally, probiotics are rarely believed to infect healthy people. Therefore, it would be preferable to determine a strain's potential for pathogenicity in advance of administration. One of the most accurate approaches is to conduct acute and chronic toxicity studies, which can also provide information about toxicity dosage. Predicting toxicity is difficult because the technique is time-consuming and infectivity is frequently strain-dependent. When probiotic strains cause infection, they are frequently undetectable in the laboratory since their long track record of safety has largely removed them from suspicion Accurate identification of *Lactobacillus* and other anaerobic probiotics in rod shape is challenging, as most commercial identification systems are inadequate for this particular bacterium. Microscopic detection also proved difficult. For example, the morphology of *Lactobacillus* is similar to other genera, including *Corynebacterium*, *Clostridium*, *Nocardia*, and *Streptococcus*. Based on gram stain detection, probiotics such as *Lactobacillus* were mistaken for diphtheroids and thus dismissed as contaminants.Similarly, *Enterococcus spp.* has been confused with *Weissella confusa* because they are both pyroglutamyl aminopeptidase positive and may have similar morphology based on Gram stain results of blood agar plates.Detailed identification, for example using specific polymerase chain reaction and pulsed-field gel electrophoresis, is usually required.

1.12 Application of Probiotics:

1.12.1 Clinicalapplicationof probiotics:

Along with stomach issues, probiotics can help with a variety of acute and chronic infectious diseases. as shown inthefigureno.6. Thebody'sdefensescanbeweakenedbyavarietyoffactors,leadingtoinflammatory,viral, neoplastic, and degenerative diseases. Other therapies, such as antibiotics, radiation, and immunosuppressive therapy,maychangethestomach'snormalfloracomposition.Thegoaloffunctionalfoodproductslikeprobiotics is to improve cellular well-being and accelerate the implementation of cells' natural defense mechanisms.

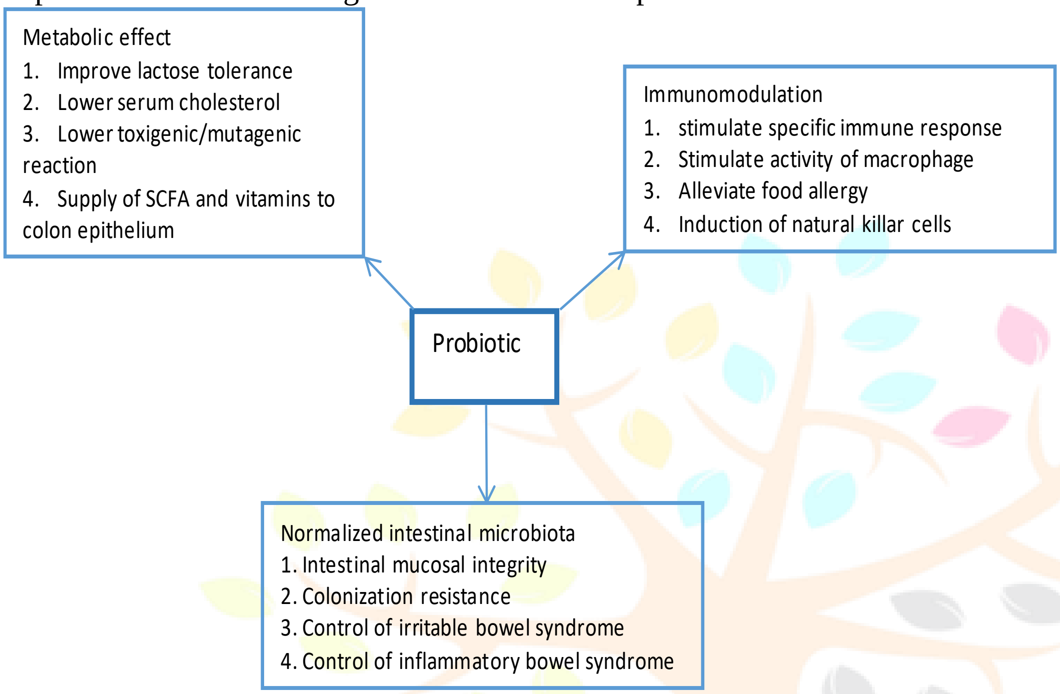


Fig.6:ClinicalApplicationofProbiotics

Probiotics' effects on human disease, diseases, mood, behaviors, and performance have been the subject of numerousstudies.Thetreatmentplanshouldincludepharmacologicaltherapy,dietaryrecommendations,andthe useofcomplementarymedicineslikeprobiotics.Probioticsareapromisingtherapeuticandpreventiveoptionfor a variety of illnesses, including inflammatory disease, as they are known to have immune-modulatory effects on the host. Consuming probiotics in the form of powder, capsules, and drinks helps in the regeneration of the gut's beneficial microflora, which strengthens human immune systems.

1.13 **Usesofprobiotics**:

Probioticshavebeenshowntobeeffectiveinvariedclinicalconditions-rangingfrominfantilediarrhoea, necrotizing enterocolitis, antibiotic-associated diarrhoea, relapsing *Clostridium difficle* colitis, *Helicobacter pylori*infections, inflammatory bowel disease to cancer, female urogenital infection and surgical infections.

1.13.1 Recentadvance:

Probiotics can change the composition of the gut microbiota, according to some recent studies, but the exact mechanism by which they do so is still unknown. By

1) increasingregulatory Tcelldifferentiationandfunction.
2) reducingtheinflammatory response.
3) Modulatingthegutenvironment,oralprobioticsimprovedthediseasestate.
4) Enhancingthedistributionsofintestinalflora,including*Bifidobacterium*,and*Faecalibacterium* among others,thatgenerateshort-chainfattyacidsorbeneficialmetabolites.Innovativeprobioticsandprebiotics arenowmorecrucial than beforedueto thespeed at which humanmicrobiomescientificinvestigation is progressing.

1.13.1.1 Recentadvancesintheantioxidationroleof probiotics:

Nobelmechanismsofactionintheprocessofoxidation.Throughsuchanumberofmechanisms,probiotic microorganisms have been shown to have significant antioxidant abilities both in vivo and in vitro:

1) Probioticschelatemetal ions.
2) Probioticsproduce antioxidants.
3) Probioticscreateantioxidant metabolites.
4) Probioticsboosttheantioxidizeactivityofthe host.
5) Thehost'slevelsofantioxidantmetabolitesareincreasedby probiotics.
6) Probioticsregulatesignalingpathways.
7) Probioticsstoptheproduction ofreactiveoxygenspecies bytheirenzymes (ROS).
8) Probioticscontroltheintestinalbacteria.

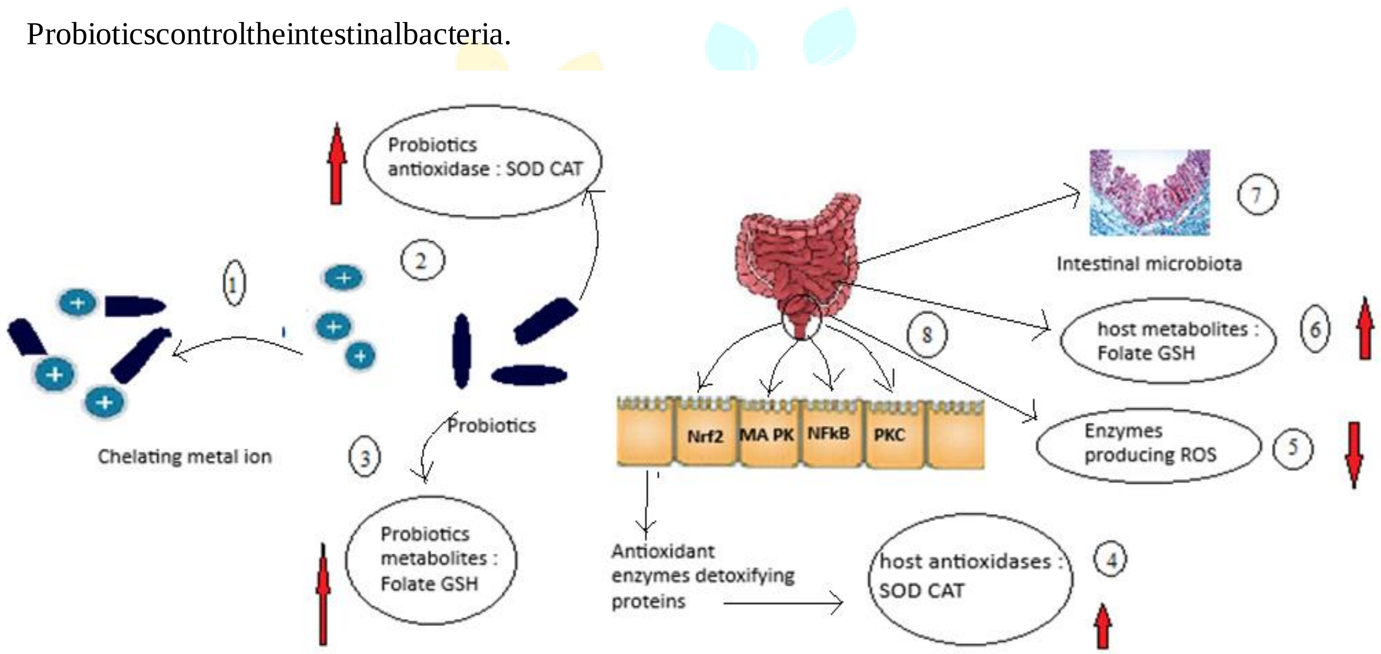


Fig.13: Nobel ModesofActionofprobioticsin antioxidation

Whenexposedtohighintensitystress,*Lacticaseibacillusrhamnosus*demonstratedsignificantantioxidant activityinhumans.Theabilityof *Lacticaseibacillusrhamnosus*toincreaseantioxidantlevelsandreduce theharmfuleffectsofreactiveoxygenspeciesmaybehelpfulforathletesexperiencingoxidativestress.

Researchoverthepastfewdecadeshasshownthatvariousprobioticbacteriastrainscanexertantioxidant activity in a number of different ways. On the basis of probiotic antioxidant mechanisms, however, not manyreviewshavebeenwrittenandpublished.Thesectionsthatfollowgiveasummaryofwhatisknown about the mechanisms of oxygen resistance in different probiotic strains as a result

1.13.2 Thetherapeuticeffect ofprobioticuseinthemanagement of hypertension:

Around the world, hypertension (HTN) has become a significant risk factor for cardiovascular, cerebrovascular,andrenaldiseases.Certaingutmicrobialstrainsmayplayapathogenicorprotectiverole intheonsetofhypertension.DysbiosisofthegutmicrobiotahasbeenlinkedtoHTNprogressioninanimal modelsandhumans,accordingtorecentresearch.LoweringluminalpH,secretingantimicrobialpeptides, blocking bacterial adhesion to epithelial cells through increased expression of intestinal mucins (MUC2) and (MUC3), enhancing mucous secretion, activating cytokine cascades and immune modulation, andinhibiting (reducing) the concentrations of myeloperoxidase, tumour necrosis factor alpha, and nuclear factor kappa are the main mechanisms by which probiotics By restricting the mucosal barrier, increasinggrowthfactorsand receptorsites,andimprovingtheGIbarrier'sintegrity, probioticscanhelp.Probiotics promote the development of non-pathogenic commensal bacteria by producing $H_2O_2$and benzoic acid, whichinhibitmanypathogenic,acid-sensitivebacteria.SCFAshaveanti-inflammatoryeffectsonimmune cells as well as bacterial colony and epithelial cells. The ability of probiotics to lower blood pressure has recently been linked to the fermentation process' production of bioactive peptides like angiotensin- converting enzyme (ACE) inhibitory peptides, which have a hypotensive effect comparable to that of ACE-inhibitor medications.

1.13.3 Production of Antibiotic Compounds

Certain probiotics have been shown to have positive effects because they can cause the host to create antimicrobial molecules that attack and destroy invasive bacteria. production of an engineered *Lactobacillus casei*that can release and produce human lactoferrin (hLF). When the hLF-expressing recombinant strain was fed to mice, histopathological examinations of the small intestine after oral treatment showed less intestinal damage and longer villi. Recombinant strains have also been developed to deal with gram-positive infections, including L. monocytogenes, an intracellular foodborne pathogen. Community bacteria have also been bioengineered to create antiviral peptides, proving they are not limited to treating bacterial infections. Targeting HIV infections at the mucosal layers of the gastrointestinal and cervico-vaginal tracts, where viral transmission predominates, results in the development of many constructions.

1.13.4 VACCINEAND DRUG DELIVERY

Besides being biological agents, recombinant probiotics are also used as delivery vehicles and effective prophylactic agents for gastroenterology. Lactamase was used as the model protein for the release of proteins from recombinant probiotics. In this study, recombinant strains of L.By delivering -lactamase to rats through lactis, the oral bioavailability was significantly enhanced, which was 2–3 times higher than the control in free solution form. Enhancing the effectiveness of this approach for delivering long-lasting drugs like insulin and growth hormones.

1.13.5 IMMUNOMODULATION

Probiotics have been developed to modulate immune responses. A number of bacteria have also been bioengineered to produce immune molecules that successfully target colitis. L. lactis secreting interleukin-27 (IL-27), anti-TNF (tumor necrosis factor), and a serine protease inhibitor, Elafin, have been shown to prevent or reduce colitis in murine models. Recombinant probiotics target allergic reactions. Modulation of acute allergic airway inflammation by IL-10-expressing L. actis has been demonstrated in a mouse model.

1.13.6 CANCER TREATMENT

Probiotic bacteria represent a new and emerging class of biotherapeutic agents for colorectal cancer. The hypoxic conditions that promote tumor growth have been identified as a potential therapeutic target. Sasaki developed an enzyme prodrug therapy ,which involve administering *Bifidobacterium longum* with sequential administration of cytosine deaminases and 5-fluorocytidine (5-FC).

1.13.7 PSYCHOBIOTICS

In addition to physical benefits, probiotics can also help patients with their mental health. The gut microbiota may play a role in modulating psychological conditions such as anxiety and depression. psychobiotics I.e., a number of natural, commensal, and probiotic bacterial strains can produce and secrete psychoactive molecules such as γ-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the mammalian central nervous system. In rats, the oral administration of *Lactobacillus rhamnosus* has been shown to reduce levels of stress-induced corticosterone by modulating GABA receptor expression in the forebrain, amygdala, and hippocampus.

Conclusion

Probiotic therapy is already being used to treat a variety of illnesses, including inflammatory, allergic, neoplastic, and infectious diseases. Probiotics have an extensive range of possible uses in treating many of these ailments.

Therefore, a thorough assessment of these goods is necessary prior to implementing probiotics into regular use. A number of significant requirements and benchmarks pertaining to quality and dependability must be fulfilled. Therefore, more carefully planned, double-blind studies with reliable findings are needed to determine the actual health advantages of these products. In order for this traditional medicine to prove to be a useful instrument for medical therapy, it is crucial to carefully select the probiotic agent, standardize its dose, and have a good understanding of its helpful benefits in addition to its adverse consequences.

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