

Project on Knowledge about Probiotic among pharmacy students



Daffodil
International
University

Project On

Knowledge about Probiotic among pharmacy students

Submitted To

The Department of Pharmacy,
Faculty of Allied Health Sciences,
Daffodil International University

In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

Submitted By

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APPROVAL

This project, Knowledge about Probiotic among pharmacy students, submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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Internal Examiner 1

Internal Examiner 2

External Examiner

Project on Knowledge about Probiotic among pharmacy students

DECLARATION

I, at this moment, announce that I am carrying out this project study under the supervision of "Mr. Md. Shajib khan," Lecturer, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Impartial Compliance with the Bachelor of Pharmacy Degree Requirement (B. Pharm). This project, I declare, is my original work. I also state that neither this project nor any part thereof has been submitted for the Bachelor's award or any degree elsewhere.

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Finally, I would like to express my gratitude towards my parents and other family members for their kind cooperation and encouragement which helped me in completion of this project.

Md. Rakibul Hasan

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Author

Declaration

Dedicated to

My Parents and Supervisor...

Abstract

Probiotics are microorganisms with possible clinical benefits. They may be used to hinder and treat counter-agent poison related detachment of the insides and exceptional overwhelming the runs. They may in like manner be incredible in alleviating signs of pugnacious inside condition, and in treating atopic dermatitis in kids. Species normally used fuse *Lactobacillus sp.*, *Bifidobacterium sp.*, *Streptococcus thermophilus*, and *Saccharomyces boulardii*. The objective of this assessment was to audit pharmacy understudy to investigate their understanding into probiotics. An online outline was directed to amass data on the data for this survey. The study was driven with 11 qualified request. The online investigation was appropriated through email and electronic media stages using snowball examining. An amount of 100 part responded to the investigation. By far most of the respondents evaluated their understanding into probiotics as medium (41.4%) and extraordinary (59.9%). We acknowledge probiotics have various worthwhile effects in a wide extent of prosperity areas. So as a prosperity specialists, A medication expert need to accept the usage of probiotics properly.

Key words: Probiotic, Diarrhea, Prebiotics, synbiotics, Gene transfer, Non-alcoholic fatty liver disease (NAFLD), gastrointestinal (GI), Human Microbiome Project (HMP), Lactic acid bacteria (LAB), Toll-like receptor (TLR), Nuclear factor κ B (NF- κ B), *Lactobacillus rhamnosus* GG (LGG), Antibiotic-associated Diarrhea (AAD),

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Chapter One: Introduction

1.Introduction

Probiotics are live microorganisms progressed with claims that they give clinical benefits when consumed, generally by improving or restoring the gut flora.[1] They can be found in yogurt and other matured food sources, dietary improvements, and greatness things. Regardless of the way that people routinely consider tiny creatures and various microorganisms ruinous "germs," many are truly helpful. A couple of microorganisms help digest food, demolish disease causing cells, or produce supplements. An extensive parcel of the microorganisms in probiotic things are identical to or like microorganisms that ordinarily live in our bodies.[2] Probiotics have been used safely in food sources and dairy things for more than 100 years. Lately, there has been extending interest in their use to thwart, reduce or treat unequivocal diseases. Countless clinical fundamentals have inspected the use of probiotics for diseases going from necrotizing colitis in troublesome infants to hypertension in adults[3] The at first discovered probiotic was a certain strain of bacillus in Bulgarian yogurt, called *Lactobacillus bulgaricus*. The revelation was made in 1905 by Bulgarian specialist and microbiologist Stamen Grigorov. The high level theory, is generally credited to Nobel laureate Élie Metchnikoff, who suggested that yogurt-eating up Bulgarian workers lived longer. [4] A creating probiotics market has provoked the prerequisite for stricter necessities for intelligent approval of putative benefits introduced by microorganisms purported to be probiotic.[5] Although different affirmed benefits are advanced towards using customer probiotic things, such as decreasing gastrointestinal bother, improving safe health.[6]



Fig 1: Microscopic Probiotic.

1.1. Definition of Probiotic

An October 2001 report by the World Health Organization (WHO) portrays probiotics as "live microorganisms which when directed in acceptable wholes present a clinical benefit on the host [7][8] Following this definition, a functioning social occasion met by the Food and Agriculture Organization (FAO)/WHO in May 2002 gave the Guidelines for the Evaluation of Probiotics in Food.[9] An arrangement significance of the term probiotics, considering open information and consistent verification, was gotten after the recently referenced joint expert meeting between the FAO of the United Nations and the WHO. This effort was joined by close by authoritative and supragovernmental managerial bodies' requirements to all the more promptly depict prosperity claims approvals. That first overall effort was also developed in 2010; two expert social events of academic specialists and industry specialists made proposition for the appraisal and endorsement of probiotic prosperity claims. [10][11] A get-together of intelligent experts gathered in London, Canada, on October 23, 2013, to discuss the expansion and legitimate use of the articulation "probiotic". That social affair was awakened by upgrades in the field that followed the advancement of the 2001 definition, and the board's choices were appropriated in June 2014[12] The articulation "probiotic" is now and again inaccurately used as a comparable word for putatively helpful people from commensal microbiota. The setting for this maltreatment is the assertion that particular dietary or common segments may "engage your neighborhood probiotics." Members of human commensal microbiota are as often as possible sources from which probiotics are kept, simultaneously, until such strains are separated and thereafter adequately portrayed for substance, security, and prosperity impacts, they are not probiotics. The US Food and Drug Administration (FDA) uses various terms for live microorganisms for regulatory purposes; live living beings used in animal deals with are assigned "direct-dealt with microbials"[13]

1.2. What are prebiotics and synbiotics?

The prebiotics idea was presented without precedent for 1995 by Glenn Gibson and Marcel Roberfroid. Prebiotic was depicted as "a non-absorbable food fixing that advantageously influences the host by specifically invigorating the development as well as movement of one or a set number of microorganisms in the colon, and along these lines improves have wellbeing". This definition was practically unaltered for over 15 years. As per this definition, a couple of mixtures of the sugar bunch, like short and long chain β -fructans [FOS and inulin], lactulose, and GOS, can

be delegated prebiotics. In 2008, the sixth Meeting of the International Scientific Association of Probiotics and Prebiotics (ISAPP) characterized "dietary prebiotics" as "a specifically matured fixing that outcomes in explicit changes in the creation as well as movement of the gastrointestinal microbiota, along these lines presenting benefit(s) upon have wellbeing"

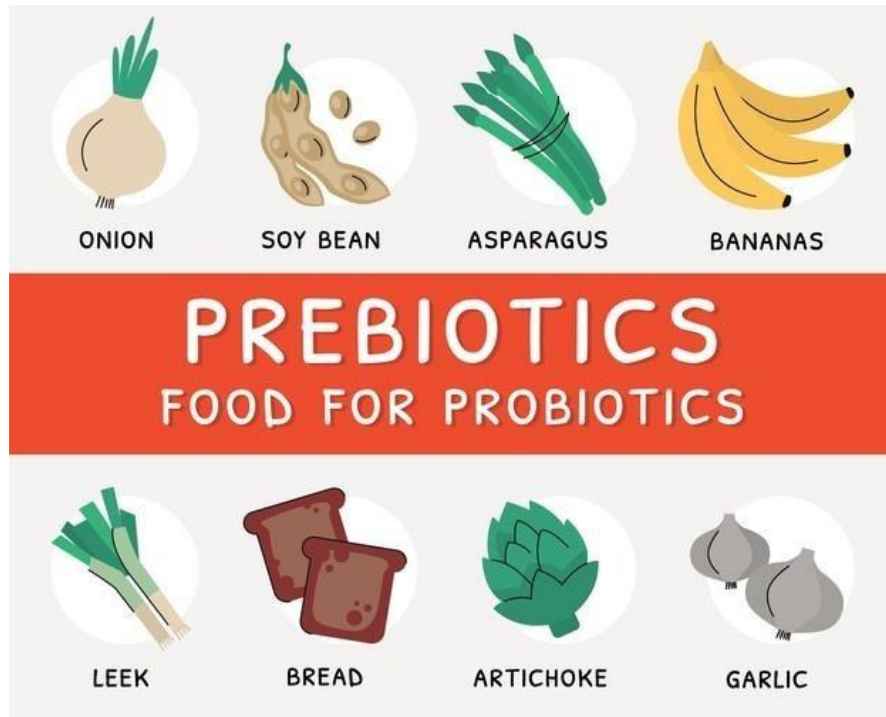


Fig 2: Prebiotics food for Probiotics.

The prebiotic goes before and helps the probiotic, and thereafter the two can unite to have a synergistic effect, known as synbiotics. A prebiotic is actually a non-digestible starch that goes about as sustenance for the probiotics and microorganisms in your gut. The significance of the effect of prebiotics is the particular instigation of advancement and moreover activity(ies) of one or a set number of microbial genus(era)/species in the gut microbiota that confer(s) clinical benefits to the host. The clinical benefits have been proposed to consolidate going probably as an answer for gastrointestinal (GI) disarrays like enteritis, blockage, and irritable inside disease; expectation and treatment of various tumors; lessening ominously defenseless disturbance; treatment of Non-alcoholic fatty liver disease (NAFLD), and engaging insusceptible inadequacy ailments. There has furthermore been research showing that the dietary confirmation of explicit food things with a prebiotic sway has been showed up, especially in young people, yet what's more likely in postmenopausal women, to construct calcium ingestion similarly as bone calcium amassing and

bone mineral thickness. The benefits for heftiness and type 2 diabetes are creating as progressing data, both from preliminary models and from human assessments, have shown explicit food things with prebiotics have impacts on energy homeostasis, satiety rule, and body weight procure. Most of the prebiotics perceived are oligosaccharides. They are impenetrable to the human stomach related synthetics that work on any leftover carbs. This infers that they go through the upper GI structure without being handled. They by then get matured in the lower colon and produce short-chain unsaturated fats that will by then support the accommodating microbiota that live there. Oligosaccharides can be consolidated or procured from ordinary sources. These sources join asparagus, artichoke, bamboo shoots, banana, grain, chicory, leeks, garlic, nectar, lentils, milk, mustards, onion, rye, soybean, sugar beet, sugarcane juice, tomato, wheat, and The clinical benefits from these oligosaccharides is a subject of ceaseless assessment.

1.2.1. Types of Prebiotics

- Fructans
- Galacto-Oligosaccharides
- Starch and Glucose-Derived Oligosaccharides
- Other Oligosaccharides
- Non-Carbohydrate Oligosaccharide

1.2.2. Prebiotics vs. Probiotics

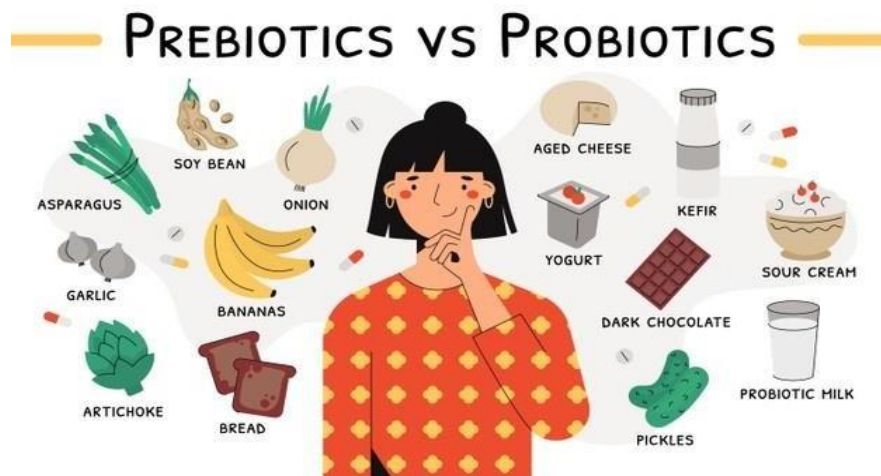


Fig 3: Prebiotics vs. Probiotics

Both prebiotics and probiotics are useful for our gut, yet they help in an unexpected way. Prebiotics are a wellspring of nourishment for our gut's solid microscopic organisms. They're carbs your body

can't process. So they go to your lower stomach related parcel, where they act like food to assist the sound microscopic organisms with developing. Probiotics are live yeasts and great microorganisms that live in your body and are useful for your stomach related framework. We can accept probiotics as enhancements or get them through food.

1.2.3. Prebiotic Foods

The prebiotics are available in many fruits, vegetables, and whole grains like:



Fig 4: Prebiotic Foods

- Apples
- Artichokes
- Asparagus
- Bananas
- Barley
- Berries
- Chicory
- Cocoa
- Dandelion greens
- Flaxseed
- Garlic
- Green vegetables
- Konjac root
- Leeks

- Legumes (peas and beans)
- Oats
- Onions
- Tomatoes
- Soybeans
- Wheat
- Yacon root

1.2.4. Benefits of Prebiotic

In addition to feeding your good gut bacteria, prebiotics can:

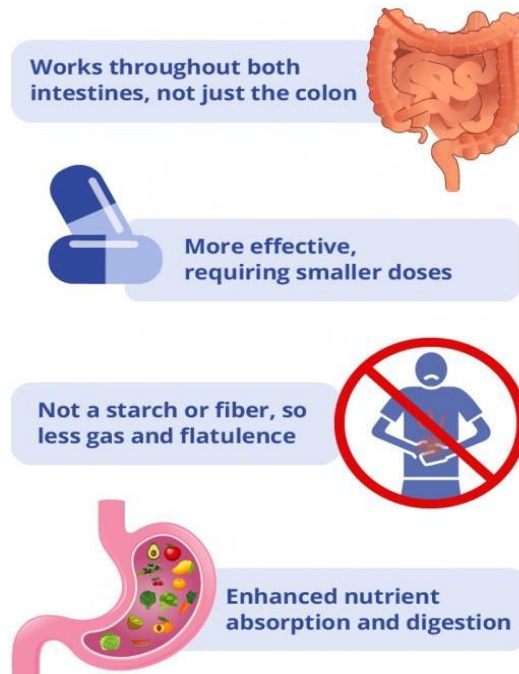


Fig 5: Benefits of Prebiotics

- Help you ingest calcium
- Change the rate at which food sources cause spikes in glucose (the glycemic list)
- Ferment food varieties quicker, so they invest less energy in your stomach related framework. That helps you not get obstructed.
- Keep the cells that line your gut solid

1.3. What are microbes and their role in our health?

Microorganisms are minimal living creatures (microorganisms, contaminations, parasites, or life forms) - so little that millions can discover a route into the kickoff of a needle - that are unbelievable to the point that a cumbersomeness in the body is related to different ailments. These microorganisms can be found in practically all parts of the human body, living on the skin, in the nose, and in the gut. There are trillions of these microorganisms in our bodies. They bantam human cells by 10 to one, anyway in view of their little size, they simply make up 1%-3% of a body's outright mass. The National Institute of Health (NIH) is supporting the Human Microbiome Project (HMP), which is making research resources for enable the examination of the microbial organizations that live in and on our bodies and the positions they play in human prosperity and ailment. The NIH has financed much more clinical examinations using HMP data and strategies, including the work of the gut microbiome in Crohn's ailment, ulcerative colitis, and esophageal harmful development; skin microbiome in psoriasis, atopic dermatitis, and immunodeficiency; urogenital microbiome in conceptive and sexual history and circumcision; and different youth issues, including pediatric stomach torture, intestinal aggravation, and necrotizing enterocolitis, a limit condition in troublesome infants wherein the stomach related plot tissue kicks the can in light of nonappearance of oxygen.

1.4. What are the different types of probiotics?

Various kinds of microorganisms are designated probiotics. They all have different benefits, yet most come from two social affairs. Get some data about which may best help you.

- Lactobacillus may be the most broadly perceived probiotic. It's the one you'll find in yogurt and other matured food sources. Different strains can help with detachment of the insides and may help with people who can't handle lactose, the sugar in milk.
- Bifidobacterium can be found in some dairy things. It may help work with the results of bad tempered inside issue and some various conditions.
- Saccharomyces boulardii* is a yeast found in probiotics. It appears to help fight the runs and other stomach related issues.

1.5. In food

Live probiotic social orders are fundamental for developed dairy things, other matured food assortments, and probiotic-reinforced foods.[14] Some matured things that contain Lactic acid bacteria (LAB) include: vegetables like restored vegetables, kimchi, pao cai, and sauerkraut, soy things, for instance, tempeh, miso, and soy sauce; and dairy things like yogurt, kefir, margarine milk, and non dairy things like bumble bee dust. Even more conclusively, sauerkraut contains the microorganisms *Leuconostoc mesenteroides*, *Lactobacillus plantarum*, *Pediococcus pentosaceus*, *Lactobacillus brevis*, *Leuconostoc citreum*, *Leuconostoc argentinum*, *Lactobacillus paraplantarum*, *Lactobacillus coryniformis*, and *Weissella* spp [15] Kimchi contains the organisms *Leuconostoc* spp., *Weissella* spp., and *Lactobacillus* spp. Pao cai contains *L. pentosus*, *L. plantarum*, *Leuconostoc mesenteroides*, *L. brevis*, *L. lactis*, and *L. fermentum*. A summary of various distinctive minuscule organic entities found in a couple of Asian developed results of the dirt is moreover open. [16][17] Kefir contains *Lactobacillus acidophilus*, *Bifidobacterium bifidum*, *Streptococcus thermophilus*, *Lactobacillus delbrueckii subsp. bulgaricus*, *Lactobacillus helveticus*, *Lactobacillus kefiranofaciens*, *Lactococcus lactis*, and *Leuconostoc* species [18]

1.6. Side effects

The control of the gut microbiota is awesome and may cause minuscule organic entities have interactions.[19] Though probiotics are seen as ensured, some have stresses over their prosperity in explicit cases. A couple of gathering, similar to those with immunodeficiency, short gut condition, central venous catheters, and heart valve disease, and inauspicious infants, may be at higher threat for negative events [20] In genuinely debilitated people with provocative entrail disorder, a risk exists for the section of down to earth microorganisms from the gastrointestinal part to within organs (bacterial development) as a result of bacteremia, which can cause antagonistic prosperity results. Different case reports depict scenes of defilement achieved by life structures dependable with probiotic strains in patients who consumed probiotics going before result starting. The most consistently declared single event is fungemia, with at any rate 33 reports of the presence of *Saccharomyces cerevisiae* or *Saccharomyces boulardii* (these natural substances are microbiologically hazy) in blood social orders of patients who had eaten up the probiotic *S. boulardii*. [21] Nine examples of plain sepsis have been represented [57–63], related with *S. boulardii* [cerevisiae], *Lactobacillus GG*, *Bacillus subtilis*, *Bifidobacterium breve*, or mix

probiotics. [22] Endocarditis events due to both Lactobacillus and Streptococcus probiotics have been represented as well.[23]

1.7. Consumption

In 2015, the overall retail market a motivator for probiotics was US\$41 billion, including arrangements of probiotic supplements, developed milk things, and yogurt, which alone addressed 75% of full scale consumption Innovation in probiotic things in 2015 was essentially from supplements, which made US\$4 billion and was projected to become 37% generally by 2020.[24] Consumption of yogurt things in China has extended by 20% every year since 2014. Overall consultancy firms, for instance, Mintel are driving client outlines and finding that about an enormous segment of the interviewees accomplice yogurt with expressions and articulations, for instance, "nutritious", "helps support opposition", "easy to measure" and "suitable for young people and more prepared people". Though a dairy thing, yogurt is seen as better contrasted with choices, for instance, "high-protein" milk, margarine that has "high calories, fat and cholesterol", and cheddar that has both strong and bothersome parts associated with it, a Mintel report said. "The quick advancement of yogurt shows it has gotten a primary thing in the local dairy market, or even in the whole food and reward market," said Chen Yangzhi, an examiner with Mintel [25]

1.8. History

Probiotics have gotten restored thought in the 21st century from thing creators, research studies, and clients. Their arrangement of encounters can be followed to the essential use of cheddar and matured things, that were prominent to the Greeks and Romans who proposed their use. The development of dairy food sources tends to presumably the most prepared technique for food security. Élie Metchnikoff recently proposed the opportunity of colonizing the gut with helpful microorganisms during the 20th century. The main momentum hypothesis of the positive imagined by explicit microorganisms was first introduced by Russian specialist and Nobel laureate Élie Metchnikoff, who in 1907 prescribed that it is doable to change the gut microbiota and to replace perilous life forms with important living beings. Metchnikoff, around then an educator at the Pasteur Institute in Paris, proposed the hypothesis that the developing cycle results from the development of putrefactive (proteolytic) microorganisms conveying harmful substances in the immense entrails. Proteolytic microorganisms like clostridia, which are fundamental for the standard gut microbiota, produce unsafe substances including phenols, indols, and smelling salts

from the preparing of proteins. According to Metchnikoff, these blends were liable for what he called "intestinal auto-intoxication", which would cause the real changes related with old age.[26] around at that point, milk developed with lactic-destructive tiny life forms were known to stifle the advancement of proteolytic microorganisms considering the low pH conveyed by the maturing of lactose. Metchnikoff had moreover seen that particular provincial peoples in Europe, for example in Bulgaria and the Russian steppes, who lived commonly on milk matured by lactic-destructive microorganisms, were inconceivably apparently unending. Considering these insights, Metchnikoff recommended that usage of matured milk would "seed" the stomach related parcel with harmless lactic-destructive organisms and lessening the intestinal pH, and that this would cover the improvement of proteolytic microorganisms. Metchnikoff himself introduced in his eating routine unforgiving milk matured with the organisms he called "Bulgarian Bacillus" and acknowledged his prosperity benefitted. Allies in Paris in a little while followed his model and specialists began embracing the brutal milk diet for their patients [27] Bifidobacteria were first separated from a chest dealt with child by Henry Tissier, who similarly worked at the Pasteur Institute. The separated bacterium named *Bacillus bifidus communis* [28] Tissier found that bifidobacteria are dominating in the gut microbiota of chest dealt with youngsters and he saw clinical benefits from treating infant detachment of the guts with bifidobacteria. During an erupt of shigellosis in 1917, German instructor Alfred Nissle detached a strain of *Escherichia coli* from the stool of a warrior who was not impacted by the ailment. Methods for treating compelling contaminations were needed at when against microbials were not yet free, and Nissle used the *E. coli* Nissle 1917 strain in serious gastrointestinal overpowering salmonellosis and shigellosis [29] In 1920, Rettger and Cheplin declared that Metchnikoff's "*Bulgarian Bacillus*", later called *Lactobacillus delbrueckii subsp. bulgaricus*, couldn't live in the human stomach related framework. They coordinated examinations including rodents and individuals volunteers, dealing with them with *Lactobacillus acidophilus*. They saw the disappearing of the pathogenic protist *Balantidium coli* similarly as of various gas-conveying microorganisms [30] Rettger further explored the possibilities of *L. acidophilus*, and pondered that minute living beings beginning from the gut will undoubtedly establish the ideal effect in this environment. In 1935, certain strains of *L. acidophilus* were found uncommonly unique when implanted in the human stomach related tract.[31] Contrasting counter agents poisons, probiotics were portrayed as microbially gathered elements that quicken the advancement of various microorganisms. In 1989, Roy Fuller proposed

a significance of probiotics that has been extensively used: "A live microbial feed supplement which conveniently impacts the host animal by improving its intestinal microbial harmony. Fuller's definition focuses on the need of common sense for probiotics and presents the piece of a profitable effect on the host. The articulation "probiotic" at first suggested microorganisms that affect various microorganisms. [32] The possibility of probiotics incorporated the prospect that substances released by one microorganism stimulated the improvement of another microorganism. The term was used again to portray tissue removes that enlivened microbial turn of events. The term probiotics was taken up by Parker, who portrayed the thought as, "Living things and substances that valuably influence the host animal by adding to its intestinal microbial balance." Later, the definition was fundamentally improved by Fuller. whose explanation was extraordinarily close to the definition used today. Fuller depicted probiotics as a "live microbial feed supplement which accommodatingly impacts the host animal by improving its intestinal microbial balance." He zeroed in on two huge cases for probiotics: the appropriate thought of probiotics and the capacity to help with intestinal harmony. In the following numerous years, intestinal lactic-destructive bacterial species with assumed prosperity accommodating properties were introduced as probiotics, including *Lactobacillus rhamnosus*, *Lactobacillus casei*, and *Lactobacillus johnsonii* [33]

1.9. Gene Transfer

Lactic destructive infinitesimal life forms have plasmids containing characteristics giving insurance from anti-microbial prescription, erythromycin, chloramphenicol or lincosamide, macrolide, streptomycin, and streptogramin[34] There is some verification that leuconostoc species and pediococcus species can recognize wide host range serum poison resistance plasmids from lactococcus species Conjugation move from enterococci to lactobacilli and lactococci can occur in the gut of animals similarly as in vitro; regardless, the trade to lactobacilli is very rare[35] There have furthermore been tries at sub-nuclear ID of vancomycin deterrent characteristics in lactobacilli. None were found. There is no evidence of Van A, B, H, X, Z, Y, or S by hybridization or polymerase chain reaction things Despite the theoretical possibility of equal quality trade between probiotic animals and distinctive life structures in the gut or other site, no clinical verification of move of antimicrobial resistance has anytime been seen. This is particularly crucial for note given the essential usage of probiotics correspondingly with against contamination [36]

1.10. Specificity of probiotic impacts

Disregarding the way that pooled examinations have, at times, shown colossal treatment impacts for probiotics all things considered, different probiotics can have different effects in both in vivo and in vitro assessments. The clinical or lab effects of one probiotic can't be acknowledged for another probiotic species or for different strains of comparative species. Bifidobacterium species isolated from human crap were found, in an organized investigation, to be genetically heterogeneous, and different strains had different properties to the extent destructive and oxygen strength and advancement requirements[37] This assortment in properties is likely going to provoke strain-to-strain assortment in microbiological and clinical effects. Murine examinations assert this assortment by showing an assortment of clinical effects between probiotics. Wagner et al [38] mulled over the effects of 4 assorted probiotic species (*L. reuteri*, *L. acidophilus*, *LGG*, and *B. animalis*) in preventing colonization and sepsis with *Candida albicans* in both athymic and euthymic mice. They found all strains to be guarded, anyway there were basic differences in practicality and an uncommon assortment of safe effects similarly as immunizer and proliferative responses to *C. albicans* and intestinal red hot cell infiltration. In vitro focuses moreover support the assortment of exercises of different probiotics. Indeed, one assessment showed different strains to have contradicting impacts. In an examination of dendritic cell work with the use of 2 assorted Lactobacillus species, *L. reuteri* DSM12246 was found to expressly control *L. casei* CHCC3139–impelled interleukin (IL) 12, IL-6, and tumor defilement factor α creation by murine dendritic cells and to control *L. casei* CHCC3139–started up-rule of dendritic cell costimulatory markers[39] Similarly, examinations of the effects of Bifidobacterium species on dendritic cell work have shown stepped assortment between species[40]

1.11. Probiotic systems of activity

One of the inconveniences in assessing the spot of probiotics in clinical practice is our confined understanding of their instruments of action. Regardless, a segment of the regular effects of probiotics have now been depicted, and it is huge for clinicians using probiotics to have some data on these microbiological and immunologic effects

1.12. Microbiological system

The human intestinal microbiota contains numerous different sorts of microorganisms similarly as archaea and eukarya, and the bacterial thickness is particularly high in the stomach related organ (up to 10^{11} CFU/g). In adults, the species piece radiates an impression of being consistent in a given individual as time goes on without pathologic states, for instance, infective free guts or against microbial use [41]. Regardless, considers show that probiotic minuscule living beings can basically affect the formation of the strong intestinal microbiota. For example, Sepp et al [42] treated 15 infants with 10^{10} – 10^{11} CFU LGG/d for the underlying 2 wk of life and noticed the headway of intestinal microbiota in these infant youngsters and in an untreated benchmark bunch. Using society based disclosure procedures, they found that LGG suffered in the stool at 1 more mature enough in 8 of the 15 children. There were basic differentiations in stool microbiota between the LGG-treated and control infant youngsters. In the LGG-treated infant youngsters, coliforms and lactobacilli were accessible in extended numbers as early as days 3–4 of life and, by 1 more age, *Bifidobacterium* spp. had moreover extended. The baby microbiota changes rapidly in the essential extended lengths of life and at the hour of weaning and isn't thought to reflect grown-up plans until 2 y age. Along these lines, the intestinal microbiota of children may be more agreeable to control by probiotic supplementation than that of adults. Regardless, Benno et al [43] have shown that probiotics can similarly change the intestinal microbiota of adults. They controlled LGG at a bit of 1.4×10^{10} CFU/d to 13 sound adults for 4 wk. They found that the degree of the fecal microflora tended to by bifidobacteria rose from 16.9% before LGG association to 36% after association with the use of culture-based area procedures ($P < 0.05$). There was moreover a development in lactobacilli and a decrease in the degree of the fecal microflora tended to by *Clostridium* spp. Tannock et al [44] used nuclear techniques to analyze stool bacterial peoples and found less checked changes in the adult fecal microflora during supplementation with *L. rhamnosus* DR20 than declared by various workers. Sub-nuclear profiling systems can be more strain-unequivocal than culture-based procedures and may be less uneven. In any case, either methodology for fecal profiling is confined to reflecting distal colonic luminal substance and gives little information with respect to minimal intestinal colonization. Despite these hindrances, these examinations suggest that probiotics can impact the case of microbial colonic colonization. Probiotics can in like manner impact the intestinal microbiota in disease states. A bit of the cautious parts through which they obstruct the exercises of pathogenic living beings have been clarified.

For example, in disease states related with extended intestinal mucosal permeability, it has been shown that the association of *Lactobacillus* probiotics can decrease intestinal mucosal vulnerability [45]. Probiotics produce bacteriocins, hydrogen peroxide, and biosurfactants to help their perseverance in the gastrointestinal plot and can genuinely thwart the adherence of more pathogenic microorganisms to the intestinal epithelium. Various probiotic species incite mucin creation by intestinal epithelial cells in vitro and some similarly start the making of defensin- β 2, an antimicrobial peptide. These emit an impression of being huge instruments through which some probiotic organisms act in hindering the adherence of microorganisms to the intestinal epithelium. Furthermore, such hatred of pathogenic microorganisms emits an impression of being best when probiotic strains themselves stick to the intestinal epithelium [46]. This support the possibility that probiotics need to colonize the stomach related framework to apply a profitable effect, and it is grounded that some probiotic strains do colonize the stomach related lot for >2 wk after association . This transient colonization may be sufficient to get the intestinal mucosa against colonization by more pathogenic microorganisms, animate close by and essential immune responses, and overhaul mucosal limit work. It may similarly momentarily make the fundamental microenvironment for other intestinal organic entities to flourish, with these discretionary microorganisms inciting clinical benefits. Whether or not colonization of the stomach related parcel is reliably significant for probiotics to apply their valuable effects isn't certain.[47]

1.13. Immunologic mechanisms

An extent of probiotic insusceptible effects have been portrayed, at this point direct proof for the safe instruments by which they achieve their beneficial effects is limited. Murine assessments have portrayed a part of the segments through which the intestinal microbiota redesigns intestinal epithelial limit, and this may similarly be a critical limit of probiotics. Hooper et al [48] tracked down that intestinal commensals up-direct mucinencoding characteristics in the host intestinal epithelium, which fortifies the production of natural liquid to outline a protective limit. Various inspectors have shown that Toll-like receptor (TLR) motioning by the commensal intestinal microbiota is essential for homeostasis of the intestinal epithelium and confirmation from epithelial injury. By seeing plan affirmation particles from commensal microorganisms, TLRs invigorate the formation of epithelial fix factors. This is presumably going to be a critical part through which probiotics act [49].TL Ractivation by iotas, for instance, lipopolysaccharide,

flagellin, and lipoteichoic destructive moreover makes the formation of cytokines through intracellular hailing pathways, which start record factors, for instance, nuclear factor κ B (NF- κ B). Some nonpathogenic enteric microorganisms have been appeared to immunosuppressively influence intestinal epithelial cells by clearly curbing the NF- κ B pathway [50]. Others control a comparable pathway by propelling the nuclear toll of a NF- κ B subunit, appropriately confining the length of NF- κ B commencement [51]. These inhibitory effects on the proinflammatory NF- κ B pathway may be a critical instrument by which creatures direct intestinal bothering. Clinical examinations have similarly shown some specific immunologic exercises for explicit probiotics. LGG increases mitogenstimulated and streaming unions of the relieving cytokine IL-10 when figured out how to infant youngsters [52]. LGG was furthermore found to up-direct markers of phagocyte activation in strong individuals while down-overseeing comparable markers in individuals delicate to cow milk going through cow milk challenge [53]. Unequivocal probiotics have been seemed to decrease intestinal irritation and improve intestinal mucosal permeability in ominously helpless issues for which these markers are altered. In vitro analyzes have shown probiotic exercises on dendritic cell work, which show great species-to-species assortment. For example *Bifidobacterium bifidum*, *B. longum*, or *B. pseudocatenulatum* up-oversee line blood dendritic cell IL-10 creation in vitro, however *B. infantis* doesn't. Even more lately, unequivocal probiotics have been intended to make IL-10 in the intestinal microenvironment, and future clinical examinations of such strains will be of exceptional premium [54]

1.14. Risks Associated with Probiotic Treatment

Probiotics are regularly coordinated as dietary upgrades rather than as medications or common things. Hence, there is regularly no essential to show prosperity, ideals, or force preceding advancing probiotics. This can incite tremendous abnormalities between the communicated and veritable substance of probiotic plans, as shown in another South African assessment [55]. In Europe, those dietary upgrades got ready for use by infants and little young people do have express compositional legitimate essentials [56]. In the United States, though dietary improvements don't all things considered require premarket study and underwriting by the Food and Drug Administration, those that are exhibited expressly for the therapy or aversion of a disorder are named characteristic things and do require review and support by the Food and Drug Administration. Additionally, in Australia, those probiotics publicized for unequivocal clinical

benefits require premarket review by the Therapeutic Goods Administration and are regularly coordinated as corresponding drugs. In Japan, those probiotic things promoted for a foreordained prosperity use moreover require formal premarket overview by the Health Ministry. Though most fiscally open probiotic strains are extensively seen as ensured, there are tremendous concerns in regards to prosperity explicitly populations.[57]

1.15. Probiotics in children

Probiotics are live microorganisms progressed with claims that they give clinical benefits when consumed, overall by improving or restoring the gut greenery. Probiotics are seen as ordinarily secured to consume, yet may cause microorganisms have associations and bothersome outcomes in unprecedented cases. There is minimal evidence that probiotics bring the clinical benefits ensured for them [58]

1.16. Health effects

1.16.1. Diarrhea

As various expectation methods for detachment of the insides have hostile effects (for instance intestinal intussusception in the utilization of rotavirus inoculation), specialists are as of now going to probiotics fully expecting using it as an improvement to treat exceptional diarrhea.[59] In an overview that covered 34 hid, randomized, counterfeit therapy controlled primers related to the runs and probiotics, it was contemplated that there was an overall reduction of 52% in enemy of contamination related free guts, a 8% abatement in explorer's the runs, and a 34% decline in various kinds of serious the runs. These numbers reflect a protective effect against detachment of the insides in subjects including the two adults and children. To the extent kids (age < 18 years), seven out of the 12 fundamentals drove in a clinical benefits setting showed an abatement in serious free entrails of 57%. There was no immense difference in the guarded effect of strains, to be explicit *Saccharomyces boulardii*, *Lactobacillus rhamnosus GG*, *Lactobacillus acidophilus*, and *Lactobacillus bulgaricus*. [60] Probiotics were found to be convincing in treating exceptional, overwhelming the runs in kids when a review was done in 2001, including > 700 children developed from one to four years with extreme free entrails. A 2002 review showed that *Lactobacillus* diminished the ordinary term of extraordinary detachment of the guts by 0.7 days and stool repeat by 1.6 on the second day of treatment. Estimation was best at more than ten billion

state forming units of *Lactobacillus* during the underlying 48 hours of diarrhea.[61] Moreover, there has been confirmation showing that probiotics can keep children and infant kids from gastroenteritis (in any case called stomach flu), which may in like manner make free entrails occur.

1.16.2. Antibiotic-associated diarrhea

This infection can generally be addressed by *Clostridium difficile*, a bacterium that can now and again cause genuine detachment of the entrails known as pseudomembranous colitis.[62] In a study of six primers related to serum poison related the runs in 766 children developed one month to six years, there was an overall lessening in AAD when children were dealt with probiotics. The abatement, when appeared differently in relation to counterfeit treatment, probably was from 28.5% to 11.9%; honestly, when patients were dealt with probiotics close by their part of against contamination specialists, one less determined would make AAD out of every seven. Against microbials dealt with to the youths in the fundamentals included amoxicillin, penicillin and erythromycin. Evidence suggests that *S. boulardii* is best at hindering AAD in young people, *Lactobacillus GG* situating second, and a blend of *S. thermophilus* and *B. lactis* reasonably situating last. No closure can be made on how probiotics can diminish the risk of AAD from a specific sorts of against contamination. One of the proposed instruments of how probiotics safeguard from AAD is by coordinating the plan of animals in the stomach related organs. Studies including *L. acidophilus* and *Bifidobacterium* recommend that these microorganisms subdue the improvement of facultative anaerobic minuscule life forms, which will in everyday addition during against disease treatment. Likewise, it is seen that probiotics can change and prevent changes in the intestinal microflora achieved by antibiotics.[63]

1.16.3. Persistent diarrhea

A 2013 review suggested probiotics are convincing in treating tireless free entrails in kids, anyway more assessment is required. Relentless free guts is a scene that starts seriously anyway then continues for 14 days or more; In rural countries it is a huge justification bleakness and mortality in kids under five years old. The assessment showed ordinary term diminished by four days and more restricted clinical center stay; stool repeat was lessened on the fifth day.[64]

1.16.4. Allergy

Probiotics are typically given to chest dealing with mothers and their little adolescents to hinder dermatitis, yet some vulnerability exists over the strength of verification supporting this preparation [65]

1.17. Probiotics in antibacterial activity

The productive effects of probiotics have been attributed to their ability to propel the immunological and non-immunological assurance limit in the gut; normalization of extended intestinal vulnerability changed gut microflora. [66] Twelve assorted intestinal bacterial regions were limited from dim tiger shrimp [67] Among them, a bacterium, *Bacillus subtilis* strain was considered and portrayed due to unfriendly properties against three target pathogenic bacterial strains of *Vibrio alginolyticus*, *Vibrio harveyi*, and *Vibrio vulnificus* [68] Several microorganisms have been represented as pathogenic to fish. Among them, six Gram-negative shafts (*Aeromonas*, *Proteus*, *Citrobacter*, *Pseudomonas*, and *Flavobacterium Chromobacterium*) and three Gram-positive cocci (*Micrococcus* and *Streptococcus Staphylococcus*) have been represented their pathogenicity.[69]

1.18. Bioactive Compounds from Probiotic Bacteria

The fish GIT is populated with the complex microbial neighborhood. It expects a crucial part in propelling the strength of the host through the production of discretionary metabolites. Probiotic microorganisms may make sorts of assistant metabolites. The bacterial bioactive combinations are used to curb the improvement of the human fish pathogens.[70] The microbial extraction of different bioactive molecules as a huge source has served in drug revelation tries in the detachment of a couple of critical drugs.[71] The substance association of bioactive combinations of microbial beginning stage is consistently significantly unusual

1.19. Probiotic action in fish gut bacteria

The use of probiotic for land and water proficient animals is extending with the for environment-friendly practical aquaculture.[72] The gut microbiota of maritime animals is likely contained by local microbiota along with misleadingly irrefutable levels of microorganisms so kept up by their consistent ingestion from the including water.[73] Probiotic strain extended the

Project on Knowledge about Probiotic among pharmacy students

perseverance of hatchlings of the crab and *Portunus trituberculatus* moreover diminished the proportion of *Vibrio* sp. in the water used to raise the hatchlings. Henceforth, it has been represented that bacterial strains related with intestinal skin natural liquid of adult marine turbot (*Scophthalmus maximus*) contact (lima), smothered the improvement of the fish organism *V. anguillarum*. The overall completed examination uncovered that the separated *Bacillus spp.* fulfill the essential models for probiotics like destructive flexibility, bile salt strength, autoaggregation, hostile to contamination resistance, and antimicrobial activities to pitiless conditions; it might be made bacteriocin extracellular which stifles pathogenic living things. These withdraws were used for potential probiotics [74]

Chapter Two: Literature review

2.Litarature Review:

Just about a century prior, Elie Metchinkoff, a Nobel Prize champ, noticed the useful impact of lactic corrosive microorganisms in people, because of utilization of matured dairy items [75] . His perception made the establishment for the idea of 'probiotics', which has been characterized as "Live microorganisms which when directed in satisfactory sums give a medical advantage on the host" [76]. Probiotics have been accessible in the created nations for the greater part a century, at this point the medical advantages that are related with their utilization have not arrived at the radar screen of doctors in Africa, partially on the grounds that couple of items are accessible on this landmass. A huge assemblage of proof is mounting, for the utilization of probiotics for anticipation and treatment of diarrheal sicknesses [77] and for avoidance of urogenital diseases [78]. In the last case, the possibility to diminish the frequency of bacterial vaginosis (BV) is generally important in Africa, where this condition fundamentally expands the danger of HIV [79]. As of now, the helpful deadly implement for the treatment of bacterial vaginosis still remaining parts anti-toxins, with items like metronidazole, just tolerably viable against *Garduerella vaginalis*, *Mobiluncus spp* and with no impact against *Mycoplasma hominis*. As of late utilizing polymerase chain response (PCR)- denaturing slope gel electrophoresis (DGGE) and 16S rRNA sequencing, we have shown that the microbiota of most Nigerian ladies determined to have BV are overwhelmed by *Mycoplasma hominis* [80]. The annihilation of vaginal lactobacilli, strength of anaerobes, ensuing height of vaginal pH and acceptance of aggravation lead to a condition that burdens enormous quantities of ladies, in any event, when scent and release are not clear [81].

As per the 10th release of the European Pharmacopeia (2019) [82], 'live bio-therapeutic items' for human use are restorative items containing live microorganisms that can be controlled orally or vaginally in different drug structures. New terms, for example, 'para-probiotic' or 'post-biotic' have arisen to signify that non-suitable microbial cells, microbial divisions, or cell lysates may likewise offer physiological advantages to the host by giving extra bioactivity [83]. Then again, 'prebiotics' are substrates that are specifically utilized by have microorganisms giving a medical advantage [84], and 'synbiotics' are dietary enhancements or food fixings that consolidate the effects of probiotics and prebiotics [85]. Regardless of the broad and effectively available proof that upholds the advantages of probiotic use, wellbeing experts may waver in prescribing probiotics to patients when they get inconsistent signals. Wellbeing experts may have difficult in preparing huge

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volumes of data created by business endeavors about the advantages and utilization of probiotics. In view of Regulation No. 1924/2006 of the European Union on sustenance and wellbeing claims made on food sources [86], EU part states have illegal the utilization of the term 'probiotic' on all food varieties including probiotic food supplements except if the techniques noted in the guideline have been noticed. This can prompt impressive disarray among wellbeing experts while instructing patients on the utilization concerning probiotics. In this way, our point was to examine the current information, mentality, and practice of wellbeing experts with respect to probiotics.

Chapter Three: Goal of my studies

Goal of my studies:

The possibility that microbes are helpful can be hard to comprehend. We take anti-infection agents to murder unsafe bacterial diseases and utilize antibacterial cleansers and moisturizers like never before. Some unacceptable microbes in some unacceptable spot can cause issues, however the correct microscopic organisms in the opportune spot can have benefits. This is the place where probiotics come in. Probiotics are live microorganisms that might have the option to help forestall and treat a few diseases. Advancing a solid stomach related lot and a sound insusceptible framework are their most broadly considered advantages right now. These are likewise regularly known as agreeable, great, or sound microorganisms. Probiotics can be provided through food sources, refreshments, and dietary enhancements.

My targets of this examinations is given underneath:

1. My plan to see, the knowledge about probiotic among drug store understudy.
2. I need to know the knowledge about Use of supportive of biotic among drug store understudy.
3. I need to see, what amount of drug store understudy think about symptom of supportive of biotic?

Chapter Four: Methodology

4. Methodology

4.1. Knowledge about probiotic:

Probiotics are live microbes and yeasts that are useful for you, particularly your stomach related framework. We for the most part consider these germs that cause sicknesses. Be that as it may, your body is loaded with microscopic organisms, both great and awful. Probiotics are frequently called "acceptable" or "supportive" microscopic organisms since they help keep your gut solid. My plan to see, the knowledge about probiotic among drug store understudy.

4.2. Knowledge about pre-biotic and sym-biotic:

At the point when the probiotic microscopic organisms specifically mature the prebiotics in the colon, an advantageous cooperative energy has been noticed. During the metabolic interaction, that reliant relationship applies useful wellbeing impacts to the host. My object of this overview to see, the knowledge about pre-biotic and sym-biotic among drug store understudy.

4.3. Use of pro-biotic :

Probiotics are utilized to improve assimilation and reestablish ordinary vegetation. Probiotics have been utilized to treat entrails issues (like the runs, fractious gut), skin inflammation, vaginal yeast diseases, lactose prejudice, and urinary parcel contaminations. In this overview, I need to know the knowledge about Use of supportive of biotic among drug store understudy.

4.4. Location:

In geography, location or place are used to denote a regions (point, line, or area) on the earth's surface or elsewhere. The term location generally implies a higher degree of certainty than place, the latter often indicating an entity with an ambiguous boundary, relying more on human or social attributes of place identity and sense of place than on geometry. My aim to see, which area's student are more knowledgeable about probiotic.

Chapter Five: Result

Result:

5.1. Age:

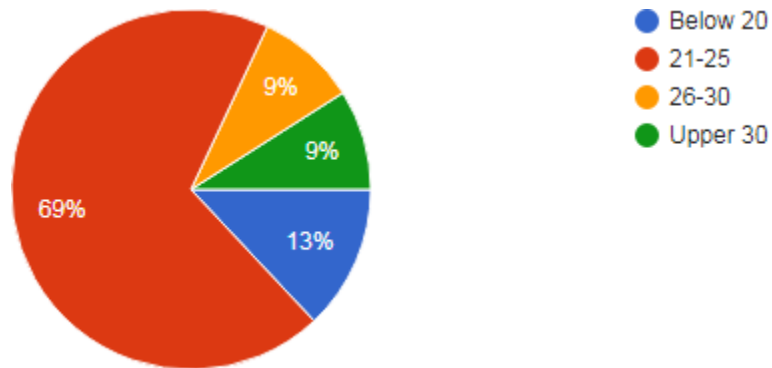


Fig 6: Participants Age

In this survey, 69% people are 21-25 years old. 9% people are upper 30 years. 9% are 26-30 years. And 13% are below 20 are participated.

5.2. Location:

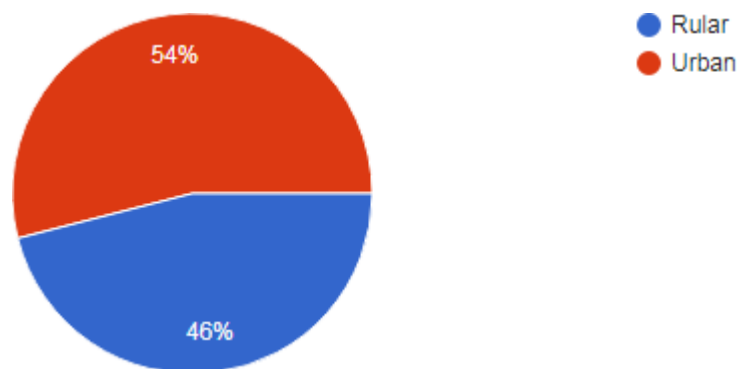


Fig 7: Participants Location

In this survey, 46% ruler and 54% urban student have knowledge about probiotic.

5.3. Level Of Education

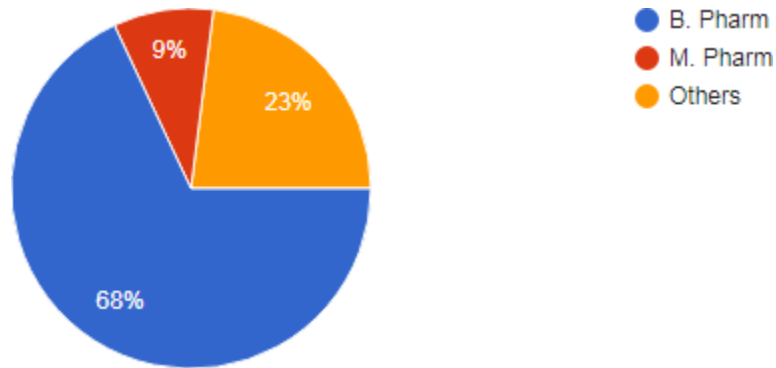


Fig 8: Level of Education

In my survey, the major part 68% people are B.pharm student. 9% are M.pharm student. And 23% are others student.

5.4. Knowledge about pro-biotic:

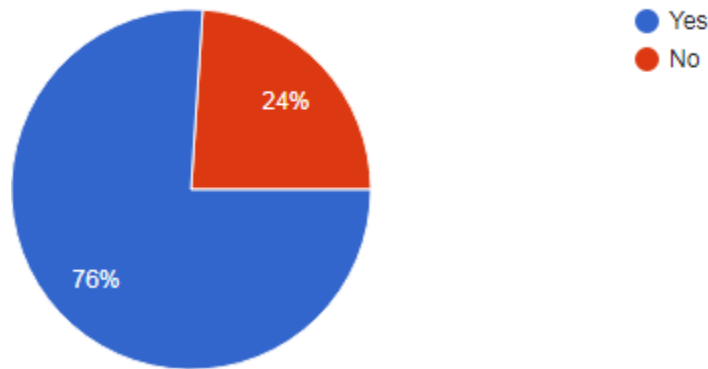


Fig 9: Knowledge about pro-biotic

According to this survey, 76% people have knowledge about probiotic and 24% people are don't know about probiotic. So, we can say, almost major part people know about probiotic.

5.5. Taking pro-biotic:

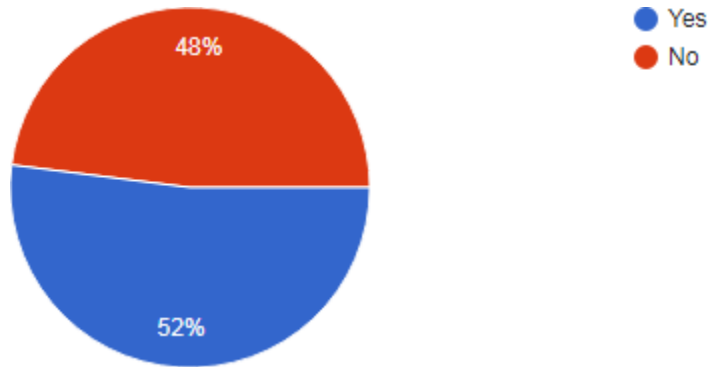


Fig 10: Taking pro-biotic

According to this survey, 52% people have taking about pro-biotic. And 48% are not take probiotic.

5.6. Side effect of probiotic:

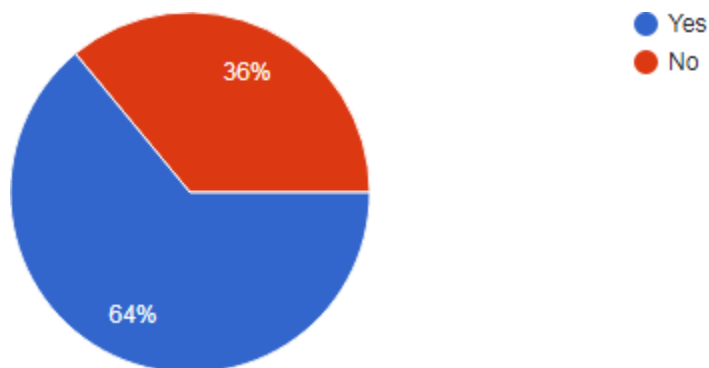


Fig 11: Side effect of probiotic

In my survey, 64% people know the side effect of probiotic. And 36% people are dont know the side effect of probiotic.

5.7. Knowledge about pre-biotic and sym-biotic:

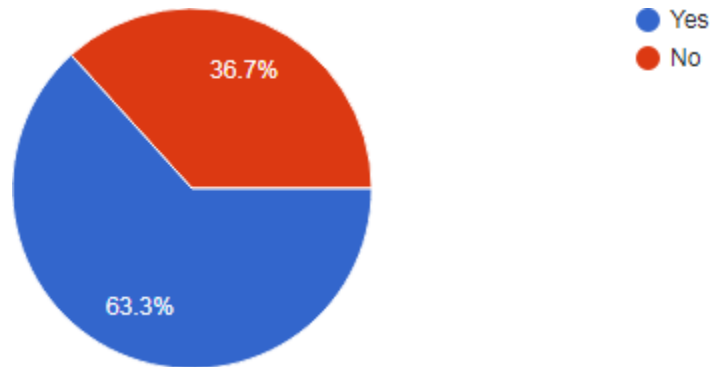


Fig 12: Knowledge about pre-biotic and sym-biotic

According to my survey, 68% people also know about pre-biotic and 36.7% people are know about sym-biotic.

5.8. Growth of harmful Bacteria:

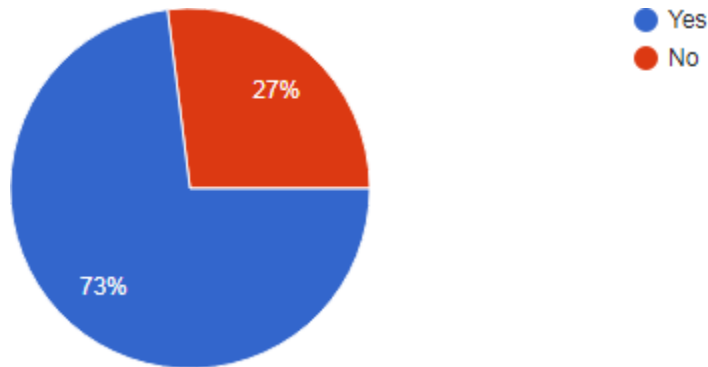


Fig 13: Growth of harmful Bacteria

In this survey, 73% people think pro-biotic can reduce the growth of harmful Bacteria. And 27% people think , it can't reduce the growth of bacteria.

5.9. Pro-biotic as diet supplemental:

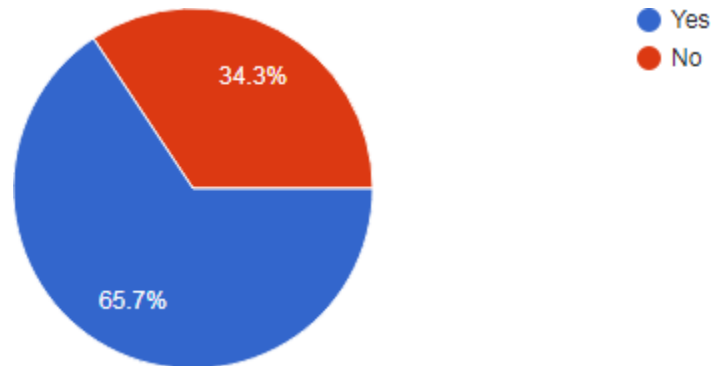


Fig 14: Pro-biotic as diet supplemental

In my survey, 65.7% people think Pro-biotic are available as diet supplemental. And 34.3% people think, it cant take as diet supplemental.

5.10. Use of probiotic in diseases:

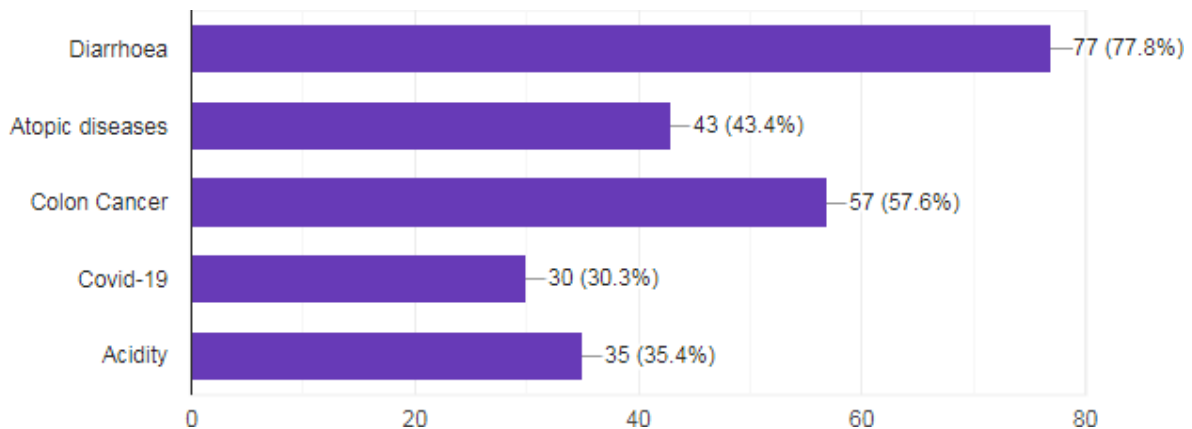


Fig 15: Use of probiotic in diseases

According to this survey, 77.8% people think probiotic are use in diarrhea. 43.4% think its use in Atopic diseases treatment. 53.6% it use for colon cancer. 30.3% people think it use to teat Covid-19. And 35.4% people think it has effect of acidity.

5.11. Taking probiotic after taking antibiotic:

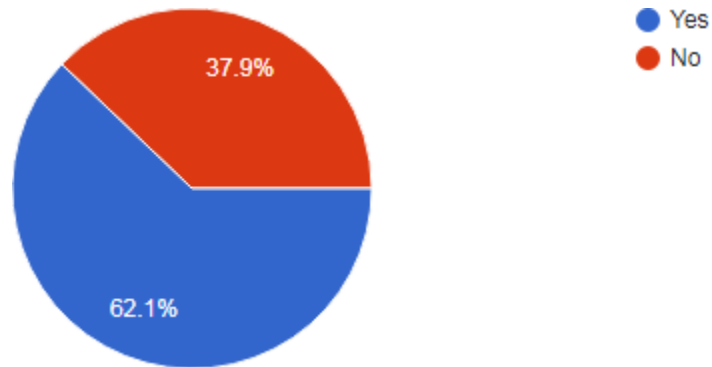


Fig 16: Taking probiotic after taking antibiotic

According to this survey, 62.1% people think, taking probiotic is important after taking antibiotic. 37.9% people think taking probiotic is not important after taking antibiotic.

5.12. Taking probiotic in a day:

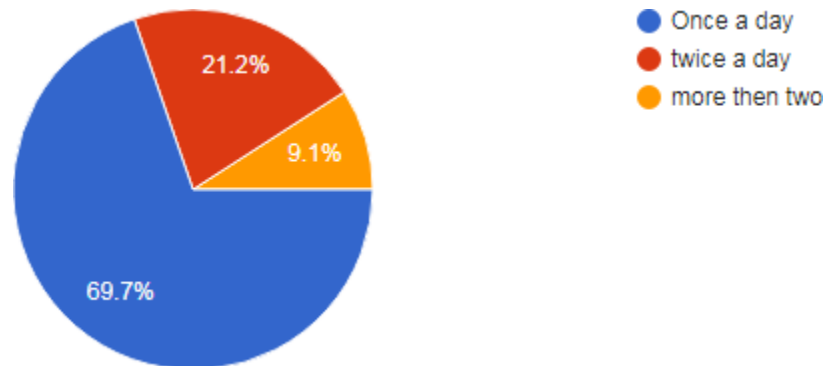


Fig 17: Taking probiotic in a day

In my survey, 69.7% people think, probiotic can take once in a day. 21.2% people think, probiotic can take twice in day. And 9.1% people think, probiotic can take more than two time in a day.

5.13. Benefits of probiotics:

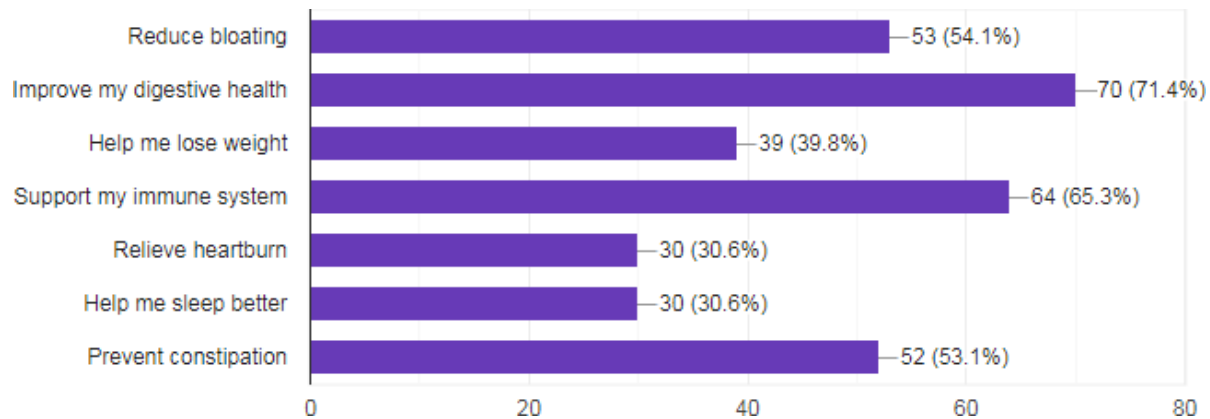


Fig 18: Benefits of probiotics

According to this survey, 54.1% think probiotic can reduce bloating. 72.4% people think , it can improve digestive health.65.3% people think it can support my immune system. And 53.1% people it can prevent constipation.

5.14. Consume probiotics:

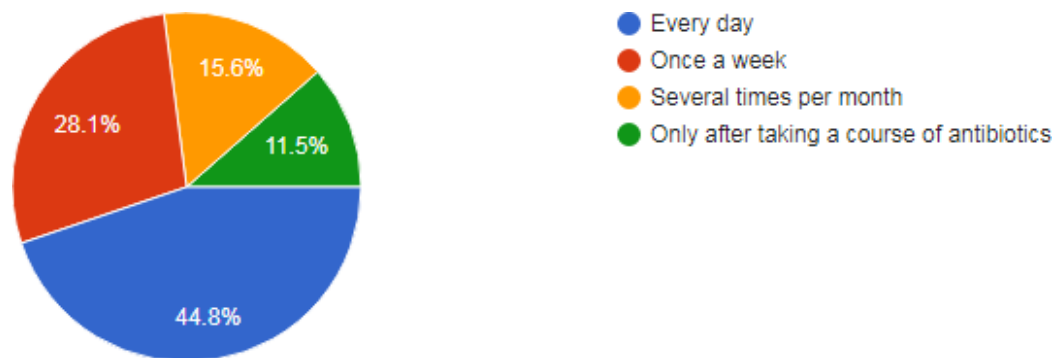


Fig 19: Consume probiotics

In this survey, 44.8% people think probiotic can take after antibiotic. 28.1% people think, it can consume once in a week. And 15.6% people think it can take per monthly.

5.15. Pro-biotic can live in human body:

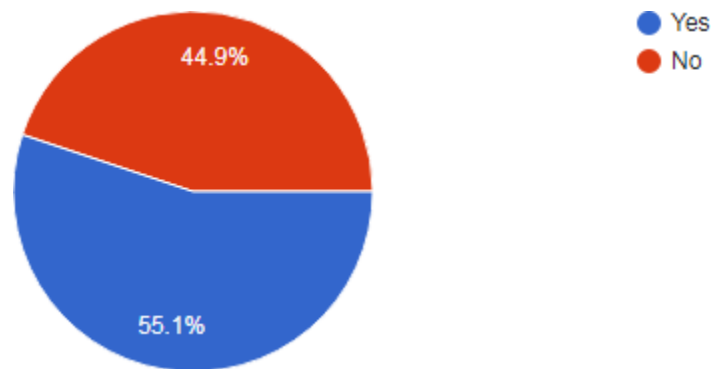


Fig 20: Pro-biotic can live in human body

In my survey, I see 55.1% people agree probiotic can live in human body. And 44.9% people are disagree with this.

Chapter Six: Conclusion

Conclusion

A few factors, for example, expanding anti-infection obstruction among pathogenic microorganisms just as the expanded requests of shoppers for common substitutes for medications have driven wellbeing experts to investigate options in contrast to drug drugs. The development of logical and clinical proof showing the effectiveness of certain probiotic strains has made them alluring as bio-therapeutics. As the current EU enactment on nourishment and wellbeing claims keeps makers from disclosing their probiotic items to the shoppers, the job of wellbeing experts in offering educated and target guidance on probiotics has generally expanded. Patients who are keen on probiotics may have difficulties finding dependable data on what probiotics do and how they really work, and may pose inquiries about probiotics when they visit their primary care physician's office. As wellbeing specialists have shown a premium in find out about probiotics, and are likewise the ones liable for getting ready different rules for probiotic utilize dependent on proof based exploration, consolidation of this point in the educational plans of future wellbeing experts and focused on learning projects of current medical services experts may help in improving their insight and mindfulness.

Chapter Seven: Reference

Project on Knowledge about Probiotic among pharmacy students

1. "Probiotics". National Health Service. 27 November 2018.
2. "Probiotics: What You Need To Know". National Center for Complementary and Integrative Health, US National Institutes of Health. 1 August 2019. Retrieved 10 November 2019
3. Bernardo WAires FT Carneiro RM et al. Effectiveness of probiotics in the prophylaxis of necrotizing enterocolitis in preterm neonates: a systematic review and meta-analysis. *J Pediatr* 2013; 89:18–24.
4. Brown, Amy C.; Valiere, Ana (2004-01-01). "Probiotics and Medical Nutrition Therapy"
5. Rijkers GT, de Vos WM, Brummer RJ, Morelli L, Corthier G, Marteau P (2011). "Health benefits and health claims of probiotics: Bridging science and marketing". *British Journal of Nutrition*. 106 (9): 1291–6.doi:10.1017/S000711451100287
6. Turck, Dominique; Castenmiller, Jacqueline; De Henauw, Stefaan; Hirsch-Ernst, Karen Ildico; Kearney, John; Knutsen, Helle Katrine; MacIuk, Alexandre; Mangelsdorf, Inge; McArdle, Harry J.; Naska, Androniki; Pelaez, Carmen; Pentieva, Kristina; Thies, Frank; Tsabouri, Sophia; Vinceti, Marco; Bresson, Jean-Louis; Siani, Alfonso (15 April 2019). "Nutrimune and immune defence against pathogens in the gastrointestinal and upper respiratory tracts: evaluation of a health claim pursuant to Article 14 of Regulation (EC) No 1924/2006"
7. Schlundt, Jorgen. "Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria" (PDF). Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. FAO / WHO. Archived from the October 22, 2012. Retrieved 17 December 2012.
8. Magdalena Araya, Catherine Stanton, Lorenzo Morelli, Gregor Reid, Maya Pineiro, et al., 2006, "Probiotics in food: health and nutritional properties and guidelines for evaluation," Combined Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria, Cordoba, Argentina, 1–4 October 2001, and Report of a Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food, London, Ontario, Canada, 30 April–1 May

2002 [FAO Food and Nutrition paper 85], pp. 1–50, Rome, Italy: World Health Organization (WHO), Food and Agriculture Organization (FAO) [of the United Nations]

9. "Guidelines for the Evaluation of Probiotics in Food" (PDF). Joint FAO/WHO Working Group on Drafting Guidelines for the Evaluation of Probiotics in Food, London, Ontario, Canada. 1 May 2002. Archived from the 2 August 2012.

10. Rijkers GT, Bengmark S, Enck P, Haller D, Herz U, Kalliomaki M, Kudo S, Lenoir-Wijnkoop I, Mercenier A, Myllyluoma E, Rabot S, Rafter J, Szajewska H, Watzl B, Wells J, Wolvers D, Antoine JM (2010). "Guidance for substantiating the evidence for beneficial effects of probiotics: current status and recommendations for future research

11. Shane AL, Cabana MD, Vidry S, Merenstein D, Hummelen R, Ellis CL, Heimbach JT, Hempel S, Lynch SV, Sanders ME, et al. (2010). "Guide to designing, conducting, publishing and communicating results of clinical studies involving probiotic applications in human participants". *Gut Microbes*. 1 (4): 243–253. doi:10.4161/gmic.1.4.12707. PMC 3023606. PMID 21327031.

12. Hill, C; Guarner, F; Reid, G; Gibson, GR; Merenstein, DJ; Pot, B; Morelli, L; Canani, RB; Flint, HJ; Salminen, S; Calder, PC; Sanders, ME (August 2014). "Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic". *Nature Reviews. Gastroenterology & Hepatology*. 11 (8): 506–14. doi:10.1038/nrgastro.2014.66. PMID 24912386

13. US Food and Drug Administration. Direct-fed microbial products Section 698.100. Revised March, 1995 Available at: http://www.fda.gov/ora/compliance_ref/cpg/cpgvet/cpg689-100.html. Accessed 18 December 2007.

14. "Technological challenges for future probiotic foods". Retrieved 29 December 2020.

15. Plengvidhya, V.; Breidt Jr, F.; Lu, Z.; Fleming, H. P. (2007). "DNA Fingerprinting of Lactic Acid Bacteria in Sauerkraut Fermentations". *Applied and Environmental Microbiology*. 73 (23): 7697–7702. doi:10.1128/AEM.01342-07. PMC 2168044. PMID 17921264.

16. Swain, Manas Ranjan; Anandharaj, Marimuthu; Ray, Ramesh Chandra; Parveen Rani, Rizwana (2014). "Fermented Fruits and Vegetables of Asia: A Potential Source of Probiotics".

Biotechnology Research International. 2014: 1–19. doi:10.1155/2014/250424. PMC 4058509. PMID 25343046

17. "Table 1: Examples of traditional fermented fruits and vegetables, which are used in various parts of Asian subcontinent". Archived from the original on 2019-02-16. Retrieved 2019-02-16.

18. Guzel-Seydim ZB, Kok-Tas T, Greene AK, Seydim AC (March 2011). "Review: functional properties of kefir". *Crit Rev Food Sci Nutr*. 51 (3): 261–8. doi:10.1080/10408390903579029. PMID 21390946. S2CID 19963871

19. Durchschein F, Petritsch W, Hammer HF (2016). "Diet therapy for inflammatory bowel diseases: The established and the new". *World J Gastroenterol (Review)*. 22 (7): 2179–94. doi:10.3748/wjg.v22.i7.2179. PMC 4734995. PMID 26900283.

20. Doron S, Snyderman DR (2015). "Risk and safety of probiotics". *Clin Infect Dis (Review)*. 60 Suppl 2: S129–34. doi:10.1093/cid/civ085. PMC 4490230. PMID 25922398. Archived from the original on 2016-08-11. Retrieved 2016-06-04.

21. Bassetti S, Frei R, Zimmerli W. Fungemia with *Saccharomyces cerevisiae* after treatment with *Saccharomyces boulardii*. *Am J Med* 1998; 105:71–2.

22. Zein EF, Karaa S, Chemaly A et al. *Lactobacillus rhamnosus* septicemia in a diabetic patient associated with probiotic use: a case report. *Ann Biol Clin (Paris)* 2008; 66:195–8.

23. Mackay AD, Taylor MB, Kibbler CC, et al. *Lactobacillus* endocarditis caused by a probiotic organism. *Clin Microbiol Infect* 1999; 5:290–2.

24. Monica Feldman (22 September 2016). "The New Market Profile of Probiotics Consumption". *Natural Products Insider*. Archived from the original on 5 September 2018. Retrieved 5 September 2018.

25. Chen Meiling (21 June 2018). "Yogurt ferments the dairy segment". *The Daily Telegraph and China Daily*. Archived from the original on 6 September 2018. Retrieved 5 September 2018.

26. Arteriosclerosis and intestinal poisons. [a contemporary review of Metchnikoff's work] *JAMA* 1910, 55:2311-12.

27. Vaughan RB (July 1965). "The romantic rationalist: A study of Elie Metchnikoff". *Medical History*. 9 (3): 201–15. doi:10.1017/S0025727300030702. PMC 1033501. PMID 14321564.
28. Tissier, H. 1900. *Recherchers sur la flora intestinale normale et pathologique du nourisson*. Thesis, University of Paris, Paris, France.
29. Altenhoefer, Artur; Oswald, Sibylle; Sonnenborn, Ulrich; Enders, Corinne; Schulze, Juergen; Hacker, Joerg; Oelschlaeger, Tobias A (April 2004). "The probiotic *Escherichia coli* strain Nissle 1917 interferes with invasion of human intestinal epithelial cells by different enteroinvasive bacterial pathogens". *FEMS Immunology & Medical Microbiology*. 40 (3): 223–229. doi:10.1016/S0928-8244(03)00368-7. PMID 15039098.
30. Cheplin HA, Rettger LF (December 1920). "Studies on the Transformation of the Intestinal Flora, with Special Reference to the Implantation of *Bacillus Acidophilus*: II. Feeding Experiments on Man". *Proceedings of the National Academy of Sciences of the United States of America*. 6 (12): 704–5. Bibcode:1920PNAS....6..704C. doi:10.1073/pnas.6.12.704. PMC 1084701. PMID 16576567.
31. Rettger, L.F., W.N. Levy, L. Weinstein, and J.E. Weiss. 1935. *Lactobacillus acidophilus* and its therapeutic application. Yale University Press, New Haven.
32. Lilly DM, Stillwell RH (1965). "Probiotics: Growth-promoting factors produced by microorganisms". *Science*. 147 (3659): 747–748. Bibcode:1965Sci...147..747L. doi:10.1126/science.147.3659.747. PMID 14242024. S2CID 26826201
33. Tannock GW (September 2003). "Probiotics: time for a dose of realism". *Current Issues in Intestinal Microbiology*. 4 (2): 33–42. PMID 14503687.
34. Lin CF, Fung ZF, Wu CL, et al. Molecular characterization of a plasmidborne (pTC82) chloramphenicol resistance determinant (cat-TC) from *Lactobacillus reuteri* G4. *Plasmid* 1996; 36:116–24.
35. Morelli L, Sarra PG, Bottazzi V. In vivo transfer of pAM beta 1 from *Lactobacillus reuteri* to *Enterococcus faecalis*. *J Appl Bacteriol* 1988; 65:371

36. Tynkkynen S, Singh KV, Varmanen P. Vancomycin resistance factor of *Lactobacillus rhamnosus* GG in relation to enterococcal vancomycin resistance (van) genes. *Int J Food Microbiol* 1998; 41:195–204
37. Matto J, Malinen E, Suihko ML, Alander M, Palva A, Saarela M. Genetic heterogeneity and functional properties of intestinal bifidobacteria. *J Appl Microbiol* 2004;97:459–70.
38. Wagner RD, Pierson C, Warner T, et al. Biotherapeutic effects of probiotic bacteria on candidiasis in immunodeficient mice. *Infect Immun* 1997;65:4165–72.
39. Christensen HR, Frokiaer H, Pestka JJ. *Lactobacilli* differentially modulate expression of cytokines and maturation surface markers in murine dendritic cells. *J Immunol* 2002;168:171–8.
40. Young SL, Simon MA, Baird MA, et al. Bifidobacterial species differentially affect expression of cell surface markers and cytokines of dendritic cells harvested from cord blood. *Clin Diagn Lab Immunol* 2004; 11:686–90.
41. Zoetendal EG, Akkermans AD, De Vos WM. Temperature gradient gel electrophoresis analysis of 16S rRNA from human fecal samples reveals stable and host-specific communities of active bacteria. *Appl Environ Microbiol* 1998;64:3854–9.
42. Sepp E, Mikelsaar M, Salminen S. Effect of *Lactobacillus casei* strain GG administration on the gastrointestinal microbiota of newborns. *Microbial Ecol Health Dis* 1993;6:309–14
43. Benno Y, He F, Hosoda M. Effects of *Lactobacillus* GG yoghurt on RISKS OF PROBIOTIC TREATMENT 1263 Downloaded from <https://academic.oup.com/ajcn/article/83/6/1256/4632996> by guest on 25 March 2021 human intestinal microecology in Japanese subjects. *Nutr Today* 1996; 31(suppl):9S–11S.
44. Tannock GW, Munro K, Harmsen HJ, Welling GW, Smart J, Gopal PK. Analysis of the fecal microflora of human subjects consuming a probiotic product containing *Lactobacillus rhamnosus* DR20. *Appl Environ Microbiol* 2000;66:2578–88.
45. Rosenfeldt V, Benfeldt E, Valerius NH, Paerregaard A, Michaelsen KF. Effect of probiotics on gastrointestinal symptoms and small intestinal permeability in children with atopic dermatitis. *J Pediatr* 2004;145: 612–6.

46. Mack DR, Ahrne S, Hyde L, Wei S, Hollingsworth MA. Extracellular MUC3 mucin secretion follows adherence of *Lactobacillus* strains to intestinal epithelial cells in vitro. *Gut* 2003;52:827–33.
47. Alander M, Satokari R, Korpela R, et al. Persistence of colonization of human colonic mucosa by a probiotic strain, *Lactobacillus rhamnosus* GG, after oral consumption. *Appl Environ Microbiol* 1999;65:351–4.
48. Hooper LV, Wong MH, Thelin A, Hansson L, Falk PG, Gordon JI. Molecular analysis of commensal host-microbial relationships in the intestine. *Science* 2001;291:881–4.
49. Rakoff-Nahoum S, Paglino J, Eslami-Varzaneh F, Edberg S, Medzhitov R. Recognition of commensal microflora by toll-like receptors is required for intestinal homeostasis. *Cell* 2004;118:229–41.
50. Neish AS, Gewirtz AT, Zeng H, et al. Prokaryotic regulation of epithelial responses by inhibition of IkappaB-alpha ubiquitination. *Science* 2000; 289:1560 –3.
51. Gaboriau-Routhiau V, Moreau MC. Gut flora allows recovery of oral tolerance to ovalbumin in mice after transient breakdown mediated by cholera toxin or *Escherichia coli* heat-labile enterotoxin. *Pediatr Res* 1996;39:625–9.
52. Wegmann TG, Lin H, Guilbert L, Mosmann TR. Bidirectional cytokine interactions in the maternal-fetal relationship: is successful pregnancy a TH2 phenomenon? *Immunol Today* 1993;14:353–6.
53. Pelto L, Isolauri E, Lilius EM, Nuutila J, Salminen S. Probiotic bacteria down-regulate the milk-induced inflammatory response in milkhypersensitive subjects but have an immunostimulatory effect in healthy subjects. *Clin Exp Allergy* 1998;28:1474 –9.
54. Steidler L, Neiryneck S, Huyghebaert N, et al. Biological containment of genetically modified *Lactococcus lactis* for intestinal delivery of human interleukin 10. *Nat Biotechnol* 2003;21:785–9.
55. Theunissen J, Britz TJ, Torriani S, Witthuhn RC. Identification of probiotic microorganisms in South African products using PCR-based DGGE analysis. *Int J Food Microbiol* 2005;98:11–21.

56. Commission of the European Communities. Commission directive on processed cereal-based foods and baby foods for infants and young children. Luxemburg City, Luxembourg: European Commission, 1996; L49:17–96.
57. FAO/WHO. Regulatory and clinical aspects of dairy probiotics. Cordoba, Argentina: FAO/WHO, 2001.
58. Durchschein F, Petritsch W, Hammer HF (2016). "Diet therapy for inflammatory bowel diseases: The established and the new". *World J Gastroenterol (Review)*. 22 (7): 2179–94. doi:10.3748/wjg.v22.i7.2179. PMC 4734995. PMID 26900283
59. Huang, J. S.; Bousvaros, A.; Lee (2002). "Efficacy of Probiotic Use in Acute Diarrhea in Children: A Meta-analysis". *Digestive Diseases and Sciences*. 47 (11): 2625–2634. doi:10.1023/A:1020501202369. PMID 12452406. S2CID 207559325
60. Sazawal, S.; Hiremath, G.; Dhingra, U.; Malik, P.; Deb, S.; Black, R. E. (2006). "Efficacy of Probiotics in Prevention of Acute Diarrhoea: a Meta-analysis of Masked, Randomized, Placebo-controlled Trials". *Lancet Infectious Diseases*. 6 (6): 374–382. doi:10.1016/s1473-3099(06)70495-9. PMID 16728323.
61. Szajewska, H.; Mrukowicz, J. (2001). "Probiotics in the Treatment and Prevention of Acute Infectious Diarrhea in Infants and Children: A Systematic Review of Published Randomized, Double-Blind, Placebo-Controlled Trials". *Journal of Pediatric Gastroenterology and Nutrition*. 33 (2): S17–S25.
62. Bartlett, J. G.; Chang, T. W.; Gurwith, M.; Gorbach, S.; Onderdonk, A. B. (1987). "Antibiotic-associated Pseudomembranous Colitis due to Toxin-producing Clostridia". *The New England Journal of Medicine*. 298 (10): 531–534. doi:10.1056/nejm197803092981003. PMID 625309.
63. Szajewska, H.; Mrukowicz, J. (2001). "Probiotics in the Treatment and Prevention of Acute Infectious Diarrhea in Infants and Children: A Systematic Review of Published Randomized, Double-Blind, Placebo-Controlled Trials". *Journal of Pediatric Gastroenterology and Nutrition*. 33 (2): S17–S25. doi:10.1097/00005176-200110002-00004. PMID 11698781. S2CID 2648000
64. Bernaola Aponte, G; Bada Mancilla C; Carreazo N; Rojas Galarza R (August 2013). "Probiotics for persistent diarrhoea in children". *Cochrane Database of Systematic Reviews* (8).

doi:10.1002/14651858.CD007401.pub3#sthash.DwpPRows.dpuf (inactive 2021-01-10).
hdl:10757/313797. Retrieved 23 September 2013.

65. Cuello-Garcia CA, Brożek JL, Fiocchi A, Pawankar R, Yepes-Nuñez JJ, Terracciano L, Gandhi S, Agarwal A, Zhang Y, Schünemann HJ (2015). "Probiotics for the prevention of allergy: A systematic review and meta-analysis of randomized controlled trials". *J. Allergy Clin. Immunol.* (Systematic review & meta-analysis). 136 (4): 952–61. doi:10.1016/j.jaci.2015.04.031. PMID 26044853.

66. Kesarcodi-Watson A, Kaspar H, Lategan MJ, Gibson L. Probiotics in aquaculture: The need, principles and mechanisms of action and screening processes. *Aquaculture* 2008;274:1-14.

67. Pandiyan P, Balaraman D, Thirunavukkarasu R, George EG, Subaramaniyan K, Manikkam S, et al. Probiotics in aquaculture. *Drug Invent Today* 2013;5:55-9.

68. Mahajan GB, Shanbhag P, Sivaramakrishnan H. Mode of Action of Antibiotic PM181104 on Bacteria, Abstract Registration No. 5SN3KNFPHL 1st Global Forum on Bacterial Infections: Balancing Treatment Access Antibiotic Resistance 2011. The Center for Disease Dynamics Economics Policy, New Delhi, India; 2011

69. Vijayaram S, Kannan S. Antagonistic activity of bacillus cereus against human and fish pathogenic bacteria. *Int J Pharm Bio Sci* 2015;6:60-8

70. Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. *J Nat Prod* 2007;70:461-77

71. Guarner F, Schaafsma GJ. Probiotics. *Int J Food Microbiol* 1998;39:237-8.

72. Nogami K, Maeda M. Bacteria as biocontrol agents for rearing larvae of the crab *Portunus trituberculatus*. *Can J Fisheries Aquatic Sci* 1992;49:2373-6

73. Nogami K, Hamasaki K, Maeda M, Hirayama K. Biocontrol method in aquaculture for rearing the swimming crab larvae *Portunus trituberculatus*. *Hydrobiologia* 1997;358:291-5.

74. Verschuere L, Rombaut G, Sorgeloos P, Verstraete W. Probiotic bacteria as biological control agents in aquaculture. *Microbiol Mol Biol Rev* 2000;64:655-71.

75. Metchnikoff, E. (1907). *The Prolongation of Life*. G.P. Putman and Sons, The Knickerbockers Press, New York, pp.221-225
76. FAO/WHO (2001). *Evaluation of Health and Nutritional Properties of Powder Milk and Live Lactic Acid Bacteria*. Food and Agriculture Organization of the United Nations and World Health Organization Report.
77. Perdone, C.A., Bernabeu, A.O., Postaire, E.R., Bouley, C.E., and Reinert, P. (1999). The effect of supplementation by *Lactobacillus casei* (Strain DN-114001) on Acute Diarrhoea in children attending day care centres. *International J. of Clinical Practice*, 53:179-184.
78. Reid, G., Bruce, A.W., Fraser, N., Heinemann, C., Owen, J., and Henning, B. (2001). Oral Probiotics can resolve Urogenital Infections. *FEMS Microbiology and Immunology*, 30:49-52.
79. Sewankambo, N., Gray, R.H., Wawer, M.J., Paxton, L., McNaim, D., Wabwire Mangen, F., Serwadda, D., Li, C., Kiwanuka, N., Hillier, S.L., Rabel, L., Gaydos, C.A., Quinn, T.C. and Konde-Lule, J. (1997). HIV-1 Infection Associated with Abnormal Vaginal Flora Morphology and Bacterial Vaginosis *Lancet*, 350 (9077): 546-50.
80. Anukam, K.C., Osazuwa, E.O., Katsivo, M.N. (2004a). Receptivity for Probiotic Products among Pre-menopausal Female Student in an African University. *Sexually Transmitted Diseases*, 31(8): 460-464.
81. Klebanoff, M.A., Schwebke, J. R., Zhang, J., Nansel, T.R., Yu, K.F., Andrews, W. W. (2004). Vulvovaginal symptoms in women bacterial Vaginosis. *Obstetrics and Gynecology*, 104(2):267-72.
82. Council of Europe. *European Pharmacopoeia*, 9th ed.; Council of Europe: Strasbourg, France, 2016; p. 6522.
83. Pandey, K.R.; Naik, S.R.; Vakil, B.V. Probiotics, prebiotics and synbiotics—A review. *J. Food Sci. Technol.* 2015, 52, 7577–7587. [CrossRef] [PubMed]
84. Gibson, G.R.; Hutkins, R.; Sanders, M.E.; Prescott, S.L.; Reimer, R.A.; Salminen, S.J.; Scott, K.; Stanton, C.; Swanson, K.S.; Cani, P.D.; et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition

Project on Knowledge about Probiotic among pharmacy students

and scope of prebiotics. *Nat. Rev. Gastroenterol. Hepatol.* 2017, 14, 491–502. [CrossRef] [PubMed]

85.Schrezenmeir, J.; de Vrese, M. Probiotics, prebiotics, and synbiotics—Approaching a definition. *Am. J. Clin. Nutr.* 2001, 73, 361s–364s. [CrossRef] [PubMed]

86.Council of Europe. *European Pharmacopoeia*, 9th ed.; Council of Europe: Strasbourg, France, 2016; p. 6522.