زانكۆى سەلاحەدین - هەولێر
Salahaddin University-Erbil

The role of commensal and probiotic bacteria in human health

Research Project

Submitted to the department of (chemistry) in partial fulfillment of the requirements for the degree of B.A or BSc. in (chemistry)

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April-2023

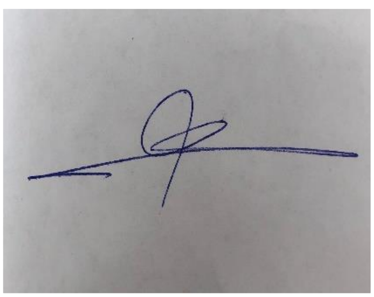
Supervisor recommendation

I am the student's supervisor, Abdullah Muhammed Ahmed. I support that the student has completed all the requirements for submitting the research drawn entitled the role of commensal and probiotic bacteria in human health according to the numbered administrative order 3/1/5/1972 on 9th oct. 2022 in accordance with the instructions of Salahaddin university quality assurance and it is ready for discussion.

(Dr. Luttfia Muhammed)

Signature with date

2023-04-06



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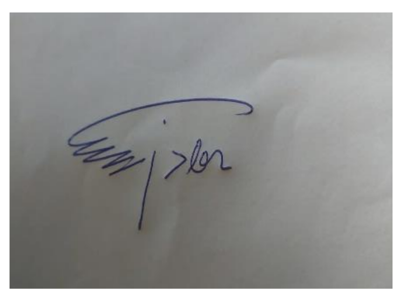

Dedication

I dedicate this project to my parents especially my mother, and my dear sisters and brothers. they always support me all the time I want to thank my family from the bottom of my heart. also, I want to thank my friends.

Acknowledgement

I am very thankful to my dear superviser Dr luttfia, she was tired with me a lot, and to the department of chemistry. also, I want to thank my project partner Gashbin faraidun, and the end I want to thank a lot to Amani Abdullah for help me to write this project.

Abstract

The human gut is one of the most complex ecosystems, composed of 1013-1014 microorganisms which play an important role in human health. In addition, some food products contain live bacteria which transit through our gastrointestinal tract and could exert beneficial effects on our health (known as probiotic effect). Among the numerous proposed health benefits attributed to commensal and probiotic bacteria, their capacity to interact with the host immune system is now well demonstrated. Currently, the use of recombinant lactic acid bacteria to deliver compounds of health interest is gaining importance as an extension of the probiotic concept. This review summarizes some of the recent findings and perspectives in the study of the crosstalk of both commensal and probiotic bacteria with the human host as well as the latest studies in recombinant commensal and probiotic bacteria. Our aim is to highlight the potential roles of recombinant bacteria in this ecosystem.and also this research include classification of bacteria and types of probiotic bacteria in general , bacteria parts , and what's prebiotic and its types , how to increase and growth of probiotic in our body , functions of probitic in our body ,sources of Probiotic bacteria and the relationship between Vitamin K and probiotic Bacteria , and how probiotic bacteria helps production and increase of vitamin K , then the relationship between Probiotic bacteria and Immune system , how helps immune system to protect our body , the effect of Anti-Biotic on Probiotic bacteria and reason of diseases .

Keyword: probiotic bacteria (gut bacteria), prebiotic, Anti-biotic, Immune system, Vitamin K.

Introduction

1.1 History of Bacteria

Nearly half a millennium ago science took a great leap forward with the discovery of the microscope. Before its existence it was postulated that "little creatures," too small to be seen by the naked eye, existed; however, it was not until the discovery of the microscope that this could be demonstrated. Two men are credited today with the discovery of microorganisms using primitive microscopes: Robert Hooke who described the fruiting structures of molds in 1665 and Antoni van Leeuwenhoek who is credited with the discovery of bacteria in 1676. Many years later, the emergence and progression of the discipline of microbiology was able to resolve two important conundrums that had prevailed in science: the existence of spontaneous generation and the nature of infectious disease.

Spontaneous generation of bacteria and other organisms was thought to be the driving process of putrefaction. This, however, was debunked by Louis Pasteur whose research on sterilization clearly indicated that this was not the case. Robert Koch's research, famously dubbed "Koch's postulates," demonstrated that infectious disease was caused by microorganisms and therefore shed light on the nature of infectious disease. The impact of the emergence of microbiology is monumental, not simply because of the scope of understanding that we have gained from its discovery, but also in terms of the increased prosperity of humans that has occurred as a result of our understanding of these "little creatures." To put the latter statement in perspective: in the year 1900 the prevailing three causes of death were influenza/pneumonia, tuberculosis and gastroenteritis, whereas in the year 2000 the prevailing causes of death were heart disease, cancer and stroke. This represents a strikingly different etiology of deaths and it will be interesting to see how these trends continue to change. (Aria Nouri,2021)

The existence of microscopic organisms was discovered during the period 1665-83 by two Fellows of The Royal Socinty, Robert Hooke and Antoni van Leeuwenhoek. In Micrographia (1665), Hooke presented the first published depiction of a microganism, the microfungus Mucor. Later, Leeuwenhoek observed and described microscopic protozoa and bacteria. These important revelations were made possible by the ingenuity of Hooke and Leeuwenhoek in fabricating and using simple microscopes that magnified objects from about 25-fold to 250-fold. After a lapse of more than 150 years, microscopy became the backbone of our understanding of the roles of microbes in the causation of infectious diseases and the recycling of chemical elements in the biosphere.(Gest, 2004)

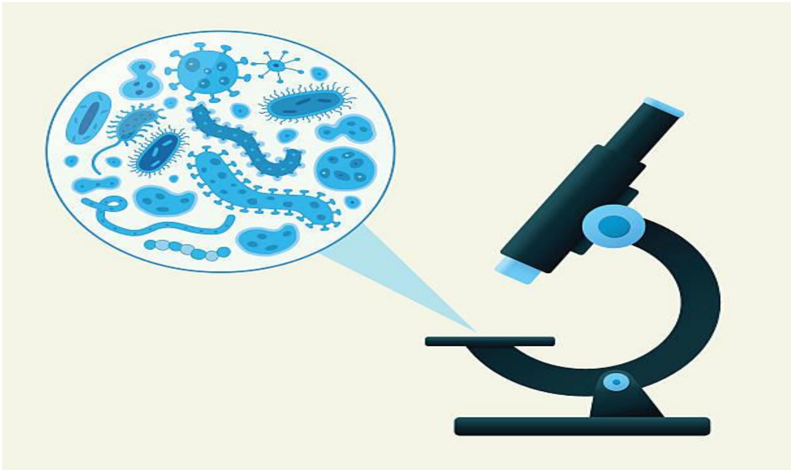

Figure 1. Bacteria under Microscope

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1.2 Classification of Bacteria

There are many different types of bacteria. One way of classifying them is by shape. There are three basic shapes.

1. Spherical: Bacteria shaped like a ball are called cocci, and a single bacterium is a coccus. Examples include the streptococcus group, responsible for “strep throat.”

2. Rod-shaped: These are known as bacilli (singular bacillus). Some rod-shaped bacteria are curved. These are known as vibrio. Examples of rod-shaped bacteria include Bacillus anthracis (B. anthracis), or anthrax.

3. Spiral: These are known as spirilla (singular spirillus). If their coil is very tight, they are known as spirochetes. Leptospirosis, Lyme disease, and syphilis are caused by bacteria of this shape.

Bacteria are often thought of as bad, but many are helpful. We would not exist without them. The oxygen we breathe was probably created by the activity of bacteria.

Many of the bacteria in the body play an important role in human survival. Bacteria in the digestive system break down nutrients, such as complex sugars, into forms the body can use. Uses Non-hazardous bacteria also help prevent diseases by occupying places that the pathogenic, or disease-causing, bacteria want to attach to. Some bacteria protect us from disease by attacking the pathogens. (Jill Seladi-Schulman and brazier, 2019)

Gut bacteria are an important component of the microbiota ecosystem in the human gut, which is colonized by 10 microbes, ten times more than the human cells. Gut bacteria play an important role in human health, such as supplying essential nutrients, synthesizing vitamin K, aiding in the digestion of cellulose, and promoting angiogenesis and enteric nerve function. However, they can also be potentially harmful due to the change of their composition when the gut ecosystem undergoes abnormal changes in the light of the use of antibiotics, illness, stress, aging, bad dietary habits, and lifestyle. Dysbiosis of the gut bacteria communities can cause many chronic diseases, such as inflammatory bowel disease, obesity, cancer, and autism. This review summarizes and discusses the roles and potential mechanisms of gut bacteria in human health and diseases. (Zhang et al., 2015)

There is a growing consensus on the beneficial effects of bifidobacteria in human health. It is now clear that bifidobacteria that exist in the large intestine are helpful for maintenance of human health and are far more important than Lactobaeillus aeidophilus as beneficial intestinal bacteria throughout human life. In other words, the reduction or disappearance of bifidobacteria in the human intestine would indicate an "unhealthy" state.

Oral administration of bifidobacteria may be effective for the improvement of intestinal flora and intestinal environment, for the therapy of enteric and hepatic disorders, for stimulation of the immune response, and possibly for the prevention of cancer and slowing the aging process. However, for consistent and positive results further well-controlled studies are urgently needed.(Mitsuoka, 1990)

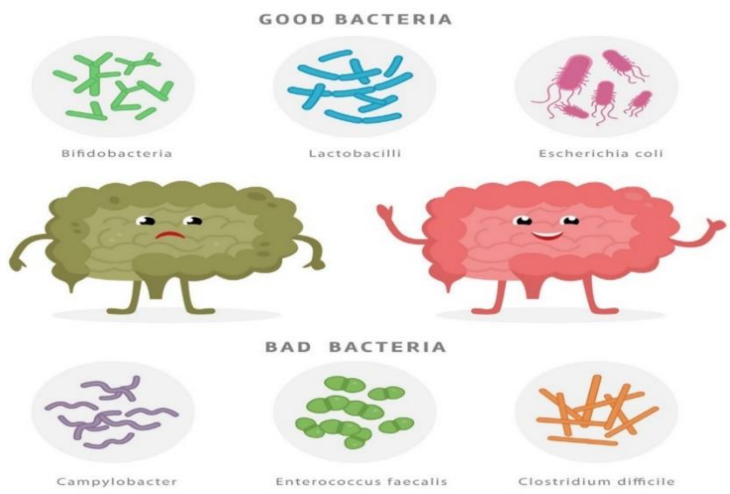

Figure 2. Classification of Bacteria

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1.3 Structure of Bacteria

Cell Wall: Cell walls of bacteria are made up of glycoprotein murein. The main function of cell wall is it helps in providing support, mechanical strength and rigidity to cell. It protects cell from bursting in a hypotonic medium.

Plasma Membrane: It is also known as cytoplasmic membrane (or) cell membrane. It is composed of phospholipids, proteins and carbohydrates, forming a fluid-mosaic. It helps in transportation of substances including removal of wastes from the body. It helps in providing a mechanical barrier to the cell. Plasma membrane acts as a semi permeable membrane, which allows only selected material to move inside and outside of the cell.

Cytoplasm: Helps in cellular growth, metabolism and replication. Cytoplasm is the store houses of all the chemicals and components that are used to sustain the life of a bacterium.

Ribosome: A tiny granule made up of RNA and proteins. They are the site of protein synthesis. They are freely floating structures that helps in transferring the genetic code.

Plasmid: Plasmids are small circle of DNA. Bacterial cells have many plasmids. Plasmids are used to exchange DNA between the bacterial cells.

Flagella: This is a rigid rotating tail. It helps the cell to move in clockwise and anticlockwise, forward and also helps the cell to spin. The rotation is powered by H+ gradient across the cell membrane.

Capsule: Capsule is a kind of slime layer, which covers the outside of the cell wall. They are composed of a thick polysaccharide. It is used to stick cells together and works as a food reserve. It protects the cell from dryness and from chemicals.(Yin et al., 2023)

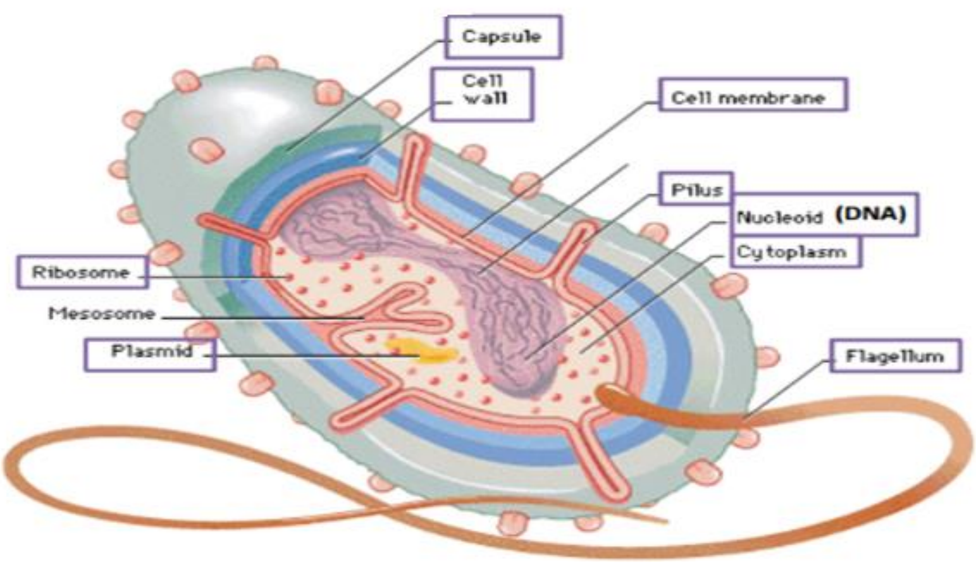

Figure 3. Structure of Bacteria (Yin et al., 2023)

1.4 History of Probiotic Bacteria

Louis Pasteur discovered fermentation by lactic acid bacteria which he described as Beneficial bacteria to protect foods from spoilage.Despite the traditional use of Fermentation in foods and beverages to impruve storage time, Safety, Functionability Organoleptic quality and nutritional properties it was Pasteur who demons started that The lactate produced during fermentation inhibited the growth of pathogens and Avoided Food spoilage.And some of the bacteria using to made vacciues and the scientific world Was shaken by the promise of modern microbiology which saw the rise of vaccines, the Isolation of beneficial bacteria and later in the century with the discovery in 1928 of Penicillin by Alexander Fleming, the development of antibiotics. Building on Louis Patens legacy, in 1899 Henri Tassier a paediatrician from the institut Pasteur discovered bifidobacterium bifidum in feal sample of breast-fed infants and reported that the bacteria couild be used to help prevent babies from developing diarrhea. An official definition was issued in 2001 by the food and agricultural organization of the united nation and the world health organization as constituting live microorganisms that, When administered In adequate amounts. Confer a health benefit on the host. In a world in constant and accelerated change and continuous inter connection, Human health is inter connected through effects of the environment, especially diet, the microbiame and the intrinsic and specific background of each individual.(Berg et al., 2020)

1.5 Prebiotic and Types of Prebiotics

prebiotics concept was introduced for the first time in 1995 by Glenn Gibson and Marcel Roberfroid. Prebiotic was described as “a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host The health”. only a few compounds of the carbohydrate group, such as short and long chain _-fructans [FOS and inulin], lactulose, and GOS, can be classified as prebiotics.

In 2008, the 6th Meeting of the International Scientific Association of Probiotics and Prebiotics (ISAPP) defined “dietary prebiotics” as “a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health”. The following criteria are used to classify a compound as a prebiotic: (i) it should be resistant to acidic pH of stomach, cannot be hydrolyzed by mammalian enzymes, and also should not be absorbed in the gastrointestinal tract, (ii) it can be fermented by intestinal microbiota this process improve hosts health.

There are many types of prebiotics. The majority of them are a subset of carbohydrate groups and are mostly oligosaccharide carbohydrates (OSCs). but there are also some pieces of evidence proving that prebiotics are not only carbohydrates.

1-Fructans: This category consists of inulin and fructo oligosaccharide or oligofructose. Their structure is a linear chain of fructose with (2-1) linkage. They usually have terminal glucose units with (2-1) linkage. the chain length of fructans is an important criterion to determine which bacteria can ferment them. Therefore, other bacterial species can also be promoted directly or indirectly by fructans.

2-Galacto-Oligosaccharides: Galacto-oligosaccharides (GOS), the product of lactose extension, are classified into two subgroups: (i) the GOS with excess galactose at C3, C4 or C6 and (ii) the GOS manufactured from lactose through enzymatic trans-glycosylation. The end product of this reaction is mainly a mixture of tri- to pentasaccharides with galactose in (1-6), (1-3), and (1-4) linkages. This type of GOS is also termed as trans-galacto-oligosaccharides or TOS.

3-non-carbohtdrate oligosaccharides: Although carbohydrates are more likely to meet the criteria of prebiotics definition, there are some compounds that are not classified as carbohydrates but are recommended to be classified as prebiotics, such as cocoa-derived flavanols. (Davani-Davari et al., 2019)

1.6 Production of prebiotics

Prebiotics play an important role in human health. They naturally exist in different dietary food products, including asparagus, sugar beet, garlic, chicory, onion, Jerusalem artichoke, wheat, honey, banana, barley, tomato, rye, soybean, human's and cow's milk, peas, beans, etc., and recently, seaweeds and microalgae. Because of their low concentration in foods, they are manufactured on industrial large scales. Some of the prebiotics are produced by using lactose, sucrose, and starch as raw material. Since most prebiotics are classified as GOS and FOS regarding industrial scale, there are many relevant studies on their production.

FOS: the concentration of FOS in these sources is not enough to have prebiotics effects. Therefore, FOS should be synthesized. There are various FOS production methods. FOS can be synthesized chemically by using glycosidase and glycosyl-transferase.The compounds that are used in these reactions are hazardous and costly, and the concentration of the end product S. cerevisiae and Zymomonas mobilis are able to eliminate small saccharides, such as glucose, fructose, and sucrose, by converting saccharides to carbon dioxide and ethanol. S. cerevisiae cannot ferment oligosaccharides with four or more monosaccharide units. Sorbitol and FOS are also produced in small amounts during fermentation of sucrose by Z. mobilis.

GOSs: were first chemically synthesized by nucleophilic and electrophilic displacement, but this method is currently deemed to be uneconomical at the industrial scale. The key enzymes for GOS formation are galactosyl-transferase and galactosidase. Galactosyl transferase is a stereoselective enzyme that can produce GOS in high quantities. Nevertheless, the bio-catalysis of GOS via galactosyl transferase is so costly, because this reaction needs nucleotide sugars as a donor. There are some approaches to decrease the cost of this reaction, such as globotriose production or using human milk oligosaccharides. (Davani-Davari et al., 2019)

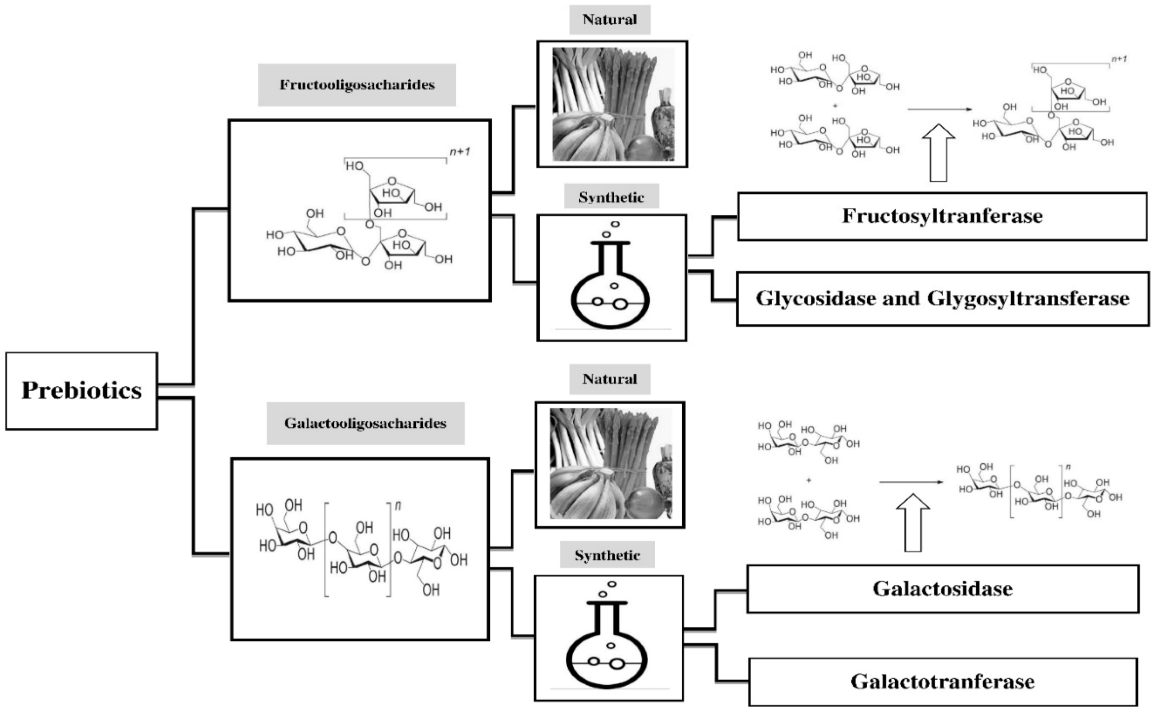

Figure 4. Sources and production of major prebiotics, including fructo oligosaccharides (FOS) and galacto-oligosaccharides (GOS). Prebiotics exist in human diets in small concentration. Since they have crucial roles in health maintenance, they are manufactured on industrial large scales. (Davani-Davari et al., 2019)

1.7 Function of Probiotic Bacteria

ability to process dietary polysaccharides, vitamin and hormone production, pH regulation, processing and detoxification of environmental chemicals, and maintenance of the skin and mucosal barrier function. In the intestine, for example, a healthymicrobial population maintains local homeostatic immune responses via exposure to bacterial structural ligands (e.g., lipopolysaccharide, LPS, and/ or peptidoglycan). The importance of gut microbes in maintaining immune system homeostasis is highlighted by the fact that the complete absence of this population in mice leads to large defects in the development of gut-associated lymph tissues, low levels of intestinal secretory IgA antibodies, and fewer and smaller mesenteric lymph nodes. Intestinal bacteria are also essential for the breakdown.

of dietary fibers, such as inulin, pectin, xylans, and mannans. This process yields energy, which is important for the growth and maintenance of the microbial community and for the production of metabolic end products that are beneficial to the host. The principal end products of carbohydrate.

processing are gases, such as CO_2, H_2, and CH_4, and short-chain fatty acids (SCFAs), such as acetate, butyrate, and propionate, which can serve as (1) important metabolites that create a direct energy source for intestinal epithelial cells, (2) inhibitors of inflammation, or (3) modulators of insulin secretion. In fact, while butyrate is an important energy source for colonic epithelial cells and an inhibitor of the NF-_B signaling that supports mucosal barrier integrity, acetate and propionate can be utilized by the liver for lipogenesis and gluconeogenesis. Intestinal microbiota can also perform multiple metabolic activities ranging from the catabolism of certain oral drugs to the synthesis of a wide range of compounds that have various effects on the host, such as several classical neurotransmitters like g-aminobutyric acid (GABA) as well as bile acids. The latter compounds, synthesized in the liver, can undergo a second conversion in the intestine via microbiota processes to generate secondary bile acids.

Ultimately, these acids can be taken up into the bloodstream, where they can potentially modulate host metabolism and other functions, including behavioral and neural functions.Thus, a complex symbiosis exists between the human body and its microbiome, the disruption of which can have detrimental effects on both. Indeed, several physiological changes (via antibiotic use and other lifestyle factors, including hygiene and diet) can strongly impact microbial composition.

The resulting dysbiosis (alteration of the microbial composition) may be unfavorable and associated with the development of the following diverse diseases .Digestive pathologies (celiac disease, inflammatory bowel disease (IBD), and nonalcoholic hepatitis) Metabolic diseases (obesity, cardiovascular diseases, and type 2 diabetes (T2D), Neurological disorders (neurodegenerative diseases and other brain disorders) Skin problems. (Scotti et al., 2017)

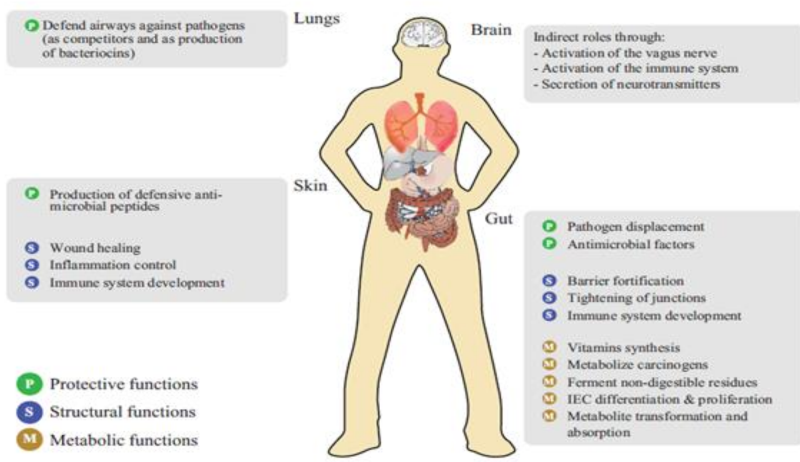

Figure 5. Probiotic Bacteria Functions (Scotti et al., 2017)

1.8 Growth and Increase of Probiotic Bacteria

Bacteria differ dramatically with respect to the conditions that are necessary for their optimal growth. In terms of nutritional needs, all cells require sources of carbon, nitrogen, sulfur, phosphorus, numerous inorganic salts (e.g., potassium, magnesium, sodium, calcium, and iron), and a large number of other elements called micronutrients (e.g., zinc, copper, manganese, selenium, tungsten, and molybdenum). Carbon is the element required in the greatest amount by bacteria since hydrogen and oxygen can be obtained from water, which is a prerequisite for bacterial growth. Also required is a source of energy to fuel the metabolism of the bacterium. One means of organizing bacteria is based on these fundamental nutritional needs: the carbon source and the energy source.

There are two sources a cell can use for carbon: inorganic compounds and organic compounds. Organisms that use the inorganic compound carbon dioxide (CO2) as their source of carbon are called autotrophs. Bacteria that require an organic source of carbon, such as sugars, proteins, fats, or amino acids, are called heterotrophs (or organotrophs). Many heterotrophs, such as Escherichia coli or Pseudomonas aeruginosa, synthesize all of their cellular constituents from simple sugars such as glucose because they possess the necessary biosynthetic pathways. Other heterotrophs have lost some of these biosynthetic pathways; in order to grow, they require that their environments contain particular amino acids, nitrogenous bases, or vitamins that are chemically intact. (BRITANICA,2020)

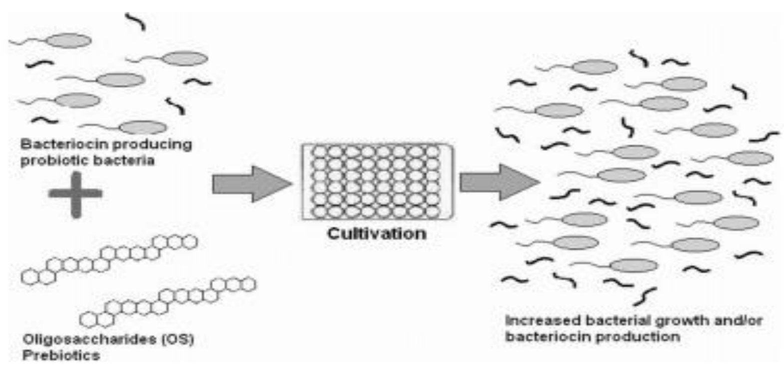

Figure 6. Growth and Increase of Probiotic Bacteria

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1.9 Source of Probiotic Bacteria

Danone was founded 100 years ago on a breakthrough concept of the time: that fermented foods and the bacteria they contained (not yet referred to as probiotics) could target the gut and its microbiome to bring health to all. One century later, Danone continues to place the gut and its microbiome at the core of its health strategy to deliver the company's mission "bringing health through food to as many people as possible". Today, the portfolio of the Danone Essential Dairy & Plant-Based division encompasses the traditional range of fermented dairy products and probiotics. The portfolio was recently broadened to include plant-based products, expanding the possibility to develop dairy and non-dairy ranges of healthy products that will contribute to nourish, enrich and protect the gut and its microbiome. Here we present the history of microbiology and Danone and reveal our research priorities for the coming years.(Veiga et al., 2020)

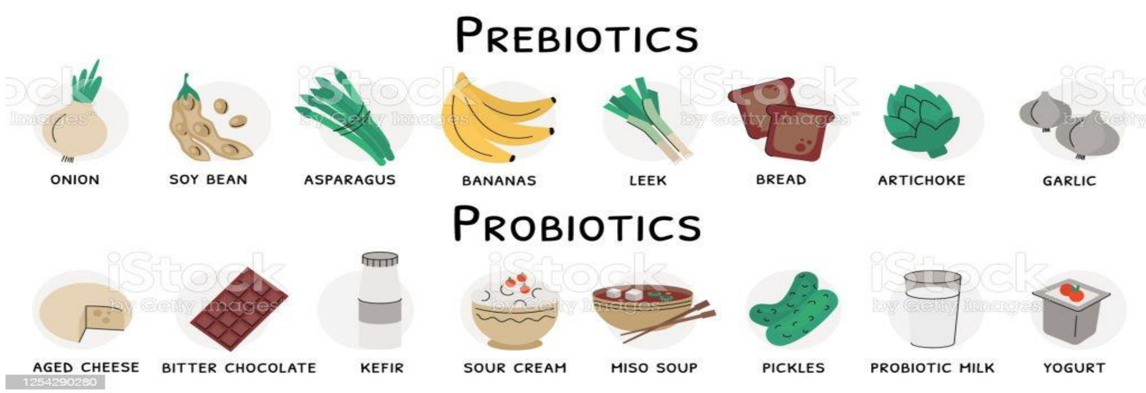

Figure 7. Source of Probiotic Bacteria

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1.10 Relationship Between Vitamin K And Probiotic Bacteria

The vitamin K antagonist is a commonly prescribed effective oral anticoagulant with a narrow therapeutic range, and the dose requirements for different patients varied greatly. In recent years, studies on human intestinal microbiome have provided many valuable insights into disease development and drug reactions. A lot of studies indicated the potential relationship between microbiome and the vitamin K antagonist. Vitamin K is absorbed by the gut, and the intestinal bacteria are a major source of vitamin K in human body. A combined use of the vitamin K antagonist and antibiotics may result in an increase in INR, thus elevating the risk of bleeding, while vitamin K supplementation can improve stability of anticoagulation for oral vitamin K antagonist treatment. Recently, how intestinal bacteria affect the response of the vitamin K antagonist remains unclear. In this review, we reviewed the research, focusing on the physiology of vitamin K in the anticoagulation treatment, and investigated the potential pathways of intestinal bacteria affecting the reaction of the vitamin K antagonist.(Yan et al., 2022)

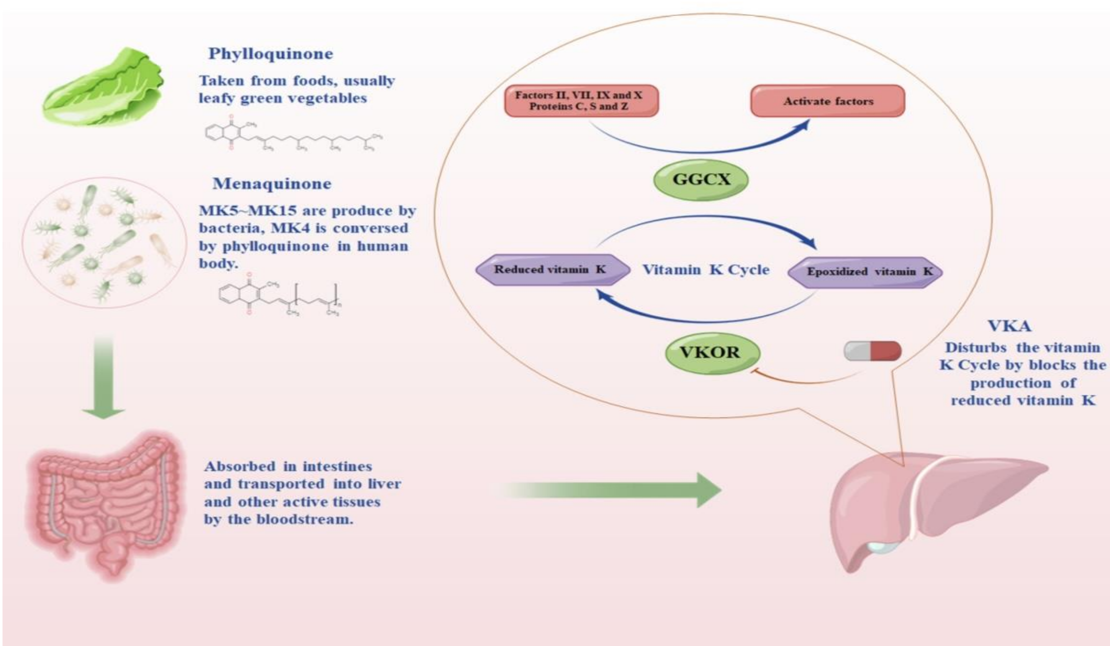

Figure 8. The source of vitamin K and the pharmacodynamic pathway of vitamin K antagonist. MKn, menaquinone, n is the number of isoprenoid units; GGCX, the gamma-glutamyl carboxylase enzyme; VKOR, vitamin K epoxide reductase. (Yan et al., 2022)

1.11 Relationship Between Immune System and Probiotic Bacteria

The gut resists pathogenic bacteria through two barriers, the mechanical barrier and the immune barrier. The mechanical barrier consists of a single layer of polarized intestinal epithelial cells, the enterocytes and mucus. On the other hand, secreted immunoglobulin A (IgA), intraepithelial lymphocytes, macrophages, neutrophils, natural killer cells, Peyer's plaques, and mesenteric lymph node compose the immune barrier.

Commensal bacteria and probiotics can promote the integrity of gut barriers. Commensal bacteria contribute to the host gut defense system mainly by resisting the invasion of pathogenic bacteria and helping the development of the host immune system. Gut bacteria maintain resistance against the colonization of pathogenic bacteria by competing for nutrients and attachment sites on the mucosal surface in the colon, a phenomenon collectively known as "colonization resistance".

The invasion of pathogenic bacteria is also prevented by commensal bacteria due to the reduction of the intestinal pH by the production of lactate and short-chain fatty acids (SCFAs). Another way is by producing toxic or carcinogenic metabolites to inhibit the growth or kill potentially pathogenic bacteria, together with volatile fatty acids that can inhibit the colonization of pathogenic bacteria. For example, proteolytic fermentation in the distal colon could produce toxic, carcinogenic metabolites such as bacteriocins, ammonia, indoles, and phenols by gut bacteria.(Martín et al., 2013)

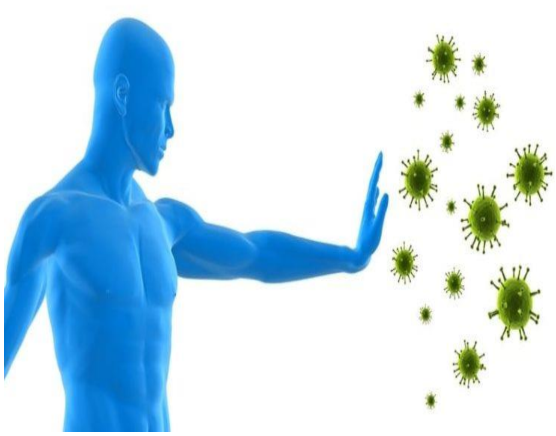

Figure 9. Probiotic Bacteria Helps Immune system to protection.

1.12 The Effect of Anti-Biotic on Probiotic Bacteria

It is well established that the gut microbiota plays an important role in host health and is perturbed by several factors including antibiotics. Antibiotic-induced changes in microbial composition can have a negative impact on host health including reduced microbial diversity, changes in functional attributes of the microbiota, formation, and selection of antibiotic-resistant strains making hosts more susceptible to infection with pathogens such as Clostridioides difficile. Antibiotic resistance is a global crisis and the increased use of antibiotics over time warrants investigation into its effects on microbiota and health. In this review, we discuss the adverse effects of antibiotics on the gut microbiota and thus host health, and suggest alternative approaches to antibiotic use.

Since their discovery, antibiotics have revolutionized the treatment of infectious diseases on a global scale. They are recognized as one of the contributing factors to increased life expectancy in the 20th century owing to the decline in infectious disease mortality. However, their overuse and misuse in human and veterinary medicine and animal husbandry have resulted in the current global antibiotic resistance crisis, which is exacerbated by the slow rate of new drug development. Despite this, antibiotics are still widely prescribed in disease treatment and studies have reported increased consumption of antibiotics in certain countries in the past number of years.

More recently, scientists have uncovered the detrimental impact of broad-spectrum antibiotics on the gut microbiota. Home to bacteria, archaea, microeukaryotes, and viruses, the gut microbiota plays a fundamental role in human health. It prevents pathogen colonization, regulates gut immunity, provides essential nutrients and bioactive metabolites, and is involved in energy homeostasis. In infants, the gut microbiota is acquired during birth and thereafter plays an essential role in the development of infant gut immunity. Evidence to date strongly suggests that balanced microbiota composition and rich species diversity are essential to its optimal functioning, which can be compromised in disease states. Likewise, reduced diversity and imbalanced microbiota composition in the infant's gut are associated with intestinal illnesses and a predisposition to certain diseases later in life.

Broad-spectrum antibiotics reduce gut microbiota diversity, and as well as killing the pathogen of concern can eradicate beneficial microbes, with deleterious MicrobiologyOpen. 2022; consequences for the host. Despite this, in Western countries, up to 35% of women are exposed to an antibiotic during pregnancy and delivery, and antibiotics comprise 80% of the drugs a woman is exposed to during pregnancy. Mothers are frequently prescribed intrapartum antibiotics prophylactically to prevent and treat infections. Clostridioides difficile (formerly known as Clostridium difficile) infection is an example of a disease brought about directly through antibiotic disruption of the gut microbiota.

Illness ranges from mild diarrhea to death. Antibiotic eradication of beneficial bacteria in the gut enables C. difficile to flourish. A recent study also concluded that oral antibiotic use is associated with an increased risk of colon cancer. These are just some of the examples of how antibiotic therapy can compromise health. This review thus focuses on the negative impacts of antibiotics on human health from pregnancy through to adulthood, most of which are microbiota-dependent, although we also provide evidence of nonmicrobiota-associated negative impacts.

We discuss the changes to microbiota composition and functionality and the consequences for host health. We look at the impact of antibiotics at the single bacterial cell level, and how antibiotic use and misuse result in antibiotic resistance development. Further, we consider alternative approaches to antibiotic therapy and discuss therapeutics that can be used to maintain and improve host health and minimize the effects of antibiotics when used. It was previously believed that infants are protected in the mother's womb which is a sterile environment, but studies have now demonstrated that amniotic fluid samples, placenta from mothers, and meconium samples from infants contain bacterial DNA suggesting the early exposure of infants to bacteria.

However, this is much debated due to issues with contamination and varying interpretations, thus we emphasize on microbiota development from infancy to adults in this review. The gut microbiota in the early stages of life becomes more diverse until it reaches a stable adult-like composition by 2–4 years of age. Following birth, the gut is colonized by facultative anaerobes due to the partially aerobic or microaerophilic environment.(Patangia et al., 2022)

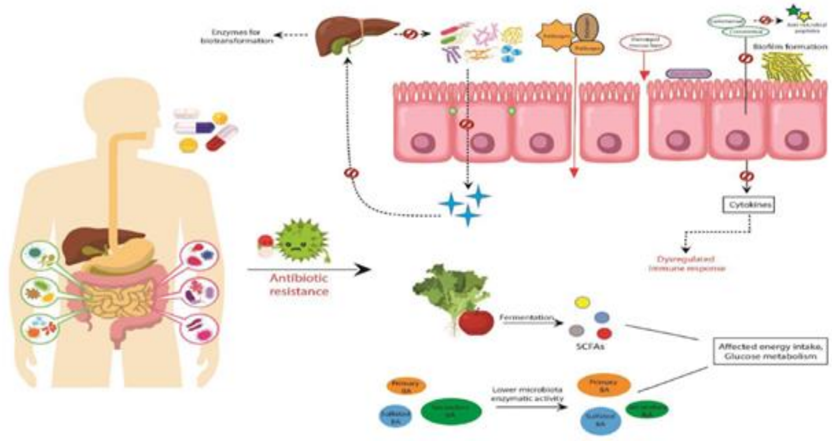

Figure 10. Effect of Anti-Biotic on Probiotic Bacteria. (Patangia et al., 2022)

Conclusion

We can conclude that current probiotic research encourages the search and characterization of gut bacteria as a model for finding new natural or engineered probiotic strains to be used to restore the normal balance of the human gut ecosystem. The fact that commensal and probiotic bacteria interact with the host immune system is now well accepted and illustrated by in vitro and in vivo experiments. However, the current knowledge of the molecular mechanisms involved in this cross-talk remain poorly understood. Although some mechanisms and active compounds have been identified in a few commensal or probiotic strains, and taking into account that the human GIT is composed of 1013-1014 microorganisms, it is necessary to explore profoundly this research area and in particular to elucidate the exact role of bacterial compounds in homeostasis and immune response. As for the use of genetically modified commensal and probiotic bacteria in humans, it is certain that most of the studies being done are Proof-of-Concept. However, although some researchers have claimed that genetically modified probiotics should be banned, the data obtained in the phase I clinical trial with the recombinant strain of L. lactis secreting IL-10 (see above in the text) showed that the containment strategy (ie. release of such genetically modified organisms into nature) used to construct the strain, was not only safe and effective but also that mucosal delivery of IL-10 by a genetically modified LAB is feasible in humans.

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