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Review Article

Exploring the microbiome: New horizons for emerging therapeutics

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ABSTRACT

The document discusses the topic of microbiomes, specifically focusing on the human microbiome and its various aspects. It starts by explaining the concept of human microbiota, which refers to the collection of microorganisms that live in and interact with the human body. The document highlights the importance of these microbial ecosystems in maintaining overall health and wellbeing. The composition and function of the gut microbiome undergo significant changes during the first year of life, especially with the introduction of solid foods. The document discusses the different bacterial phyla that dominate the gut microbiome in neonatal infants and adults. It also mentions the role of the human gut microbiome in various health conditions such as liver diseases, diabetes, inflammatory bowel disease, autoimmune diseases, colon cancer, and central nervous system disorders. The document highlights the different sequencing techniques used in microbiome research, such as ITS sequencing, PCR amplicon-based sequencing, and shotgun metagenomic sequencing. It also discusses the concept of the halobiont and holo genome in relation to the microbiome. The document emphasizes the importance of studying the microbiome in the context of ecosystem health and discusses the impact of human populations on environmental microorganisms. Furthermore, the document covers the microbial barrier in the human gut, the role of the gut microbiota in various metabolic processes, and the application of gut microbiomes in bioengineering, both in humans and other organisms. Lastly, it discusses the importance of dietary interventions, prebiotics, and the role of various diets in influencing the composition of the gut microbiome and treating gastrointestinal disorders. Overall, the document provides a comprehensive overview of the human microbiome and its significance in health and disease, as well as its potential applications in bioengineering and dietary interventions.

1. Introduction

A collection of microorganisms that live in and interact with the human body is known as the human microbiota. The different interactions could be harmful, mutualistic, or communalistic. The term "human microbiome" refers to the genetic material of microorganisms (microbiota) that live at a specific location within the human body.[1] The human body's microbial ecosystem contains 100 trillion microorganisms.[2] Numerous anatomical body locations, including the skin, mucosa, gastrointestinal system, respiratory tract, urogenital tract, and mammary gland, are colonized by microorganisms. Together, they create a distinct, sophisticated ecosystem that adjusts to the environmental requirements of every niche. A consistent relationship (symbiosis) between the human body and its natural microbiota starts with childbirth. The preservation of overall health and wellbeing is significantly influenced by these connections. The microbiota is made up of species that

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have coevolved to occupy distinct niches within the human body and actively adapt to their respective environments.[1]

Throughout the first year of life, the composition and function of the baby's gut microbiome evolve as solid foods are introduced. The transition to solid foods upsets the balance of the baby's gut ecology and offers a window of opportunity to learn about the long-term changes in the composition and function of the early infant gut microbiome. It is acknowledged that throughout the first year of life, microbial species diversify in composition. It is less evident, though, how the addition of solid foods to a diet mostly composed of milk affects the microbiome's ability to operate. At the phylum level, over 30% of Firmicutes, Bacteroidetes, and Verrucomicrobia and roughly 70% of Actinobacteria and Proteobacteria dominate the gut microbiome of neonatal infants. About 90% of Firmicutes and Bacteroidetes and 10% of Actinobacteria, Proteobacteria, and Verrucomicrobia make up the adult microbiome.[3]

In essence, humans are symbiotic creatures. Humans are essentially sterile at birth, and as they interact with microbes, they create a microbiota and strengthen their immune systems at the same time. Any multicellular organism, including plants, has a microbiota, which is described as an "assemblage of microorganisms (all the bacteria, archaea, eukaryotes, and viruses) present in a defined environment." The phrase "microbiome," which is interchangeable, can refer to the collective genomes of the microorganisms that inhabit a particular environmental niche or the individual microorganisms. Daily interactions with these microorganisms occur at the skin's surface as well as in the mouth, pharynx, urogenital tract, respiratory system, and digestive tract, which has the highest density and diversity of bacteria. Despite its proximity to the body's first immune cell pool and second neural cell pool, as well as its position at the interface between ingested food and the gut epithelium, the study of the human intestinal microbiota has languished for many years.[2] Throughout time, the host's food and age affect the gut microbiota. Numerous illnesses, including those of the liver, diabetes, inflammatory bowel disease, autoimmune diseases, colon cancer, and central nervous system disorders, are closely correlated with its state. Internal transcribed spacer (ITS) sequencing, PCR amplicon-based sequencing (e.g., 16S and 18S rRNA), shotgun metagenomic sequencing using DNA, RNA-based meta transcriptomic sequencing, and viremic sequencing are common high-throughput sequencing techniques in microbiome research. The primary methods employed in the first ten years of gut microbiome research have been shotgun metagenomic sequencing and DNA-based 16S rRNA gene sequencing, which provide information on the gene content and microbial makeup. Instead of only concentrating on bacteria, there has been a recent increase in interest in RNA-based approaches, meta transcriptomic sequencing, fungi, and viruses.[4]

According to Margulis and Fester (1991), a "halobiont" is a host and all the bacteria that are connected to it, whereas a "holo genome" is the genome of the microbes. While some scientists have questioned whether the microbiome can respond to natural selection given its low heredity, others have criticized this metaphor and believe that the halobiont is the unit upon which natural selection acts. Over the past 15 years, significant progress has been achieved in the field of microbiome research, which examines the behavior, relationships, and functions of microbial communities within a given environment. These developments have been largely fueled by the sharp decline in high-throughput screening costs and the rise in processing power over this time, which has produced an abundance of data that can be analyzed effectively on widely available hardware. Research on the microbiome today is heavily skewed towards topics related to human health. However, human health only represents one aspect of the microbiota's interaction with the environment in the larger context of ecosystem health. In actuality, the idea that a healthy ambient microbiome dictates a healthy human microbiome is becoming increasingly widely acknowledged. Studying the microbiome of ecosystems is therefore essential. The microbiome of an individual or population is influenced by the functional richness and structure of ecological communities at various biological organization sizes. Furthermore, in urbanized areas, human populations have a significant impact on the availability of environmental microorganisms in the surrounding area, leading to poorly understood non-linear feedback loops.[5]

2. Human Gut Microbiomes

The microbial barrier is made up of microorganisms that travel across the human intestine and include bacteria, viruses, fungus, bacteriophages, and protists. In a healthy state, bacteria develop distant from the enterocyte surface in the middle mucin layer. Trillions of these bacteria make up the human gut microbiota, a complex ecosystem that is found in the stomach, jejunum, terminal ileum, and colon, where there are 10^3–10^4 bacteria per gramme, 10^5–10^6 in the jejunum, 10^8–10^9 in the terminal ileum, and roughly 10^{12}–10^{14} bacteria per gramme of gut content. The gut microbiota contains at least 1000 different species of known bacteria and 150 times more microbial genes than the human genome. The gut microbiota is a component of the intricate and dynamic system known as the "intestinal barrier," which is produced by the interaction of many layers. Mucin, which is released by intestinal goblet cells and is composed of highly glycosylated proteins, makes up the second layer of the intestinal barrier. The release of gastric acid, hepatic bile, and pancreatic juice, along with gastrointestinal motility including the stomach, gallbladder, and intestine, comprise a third layer that is considered

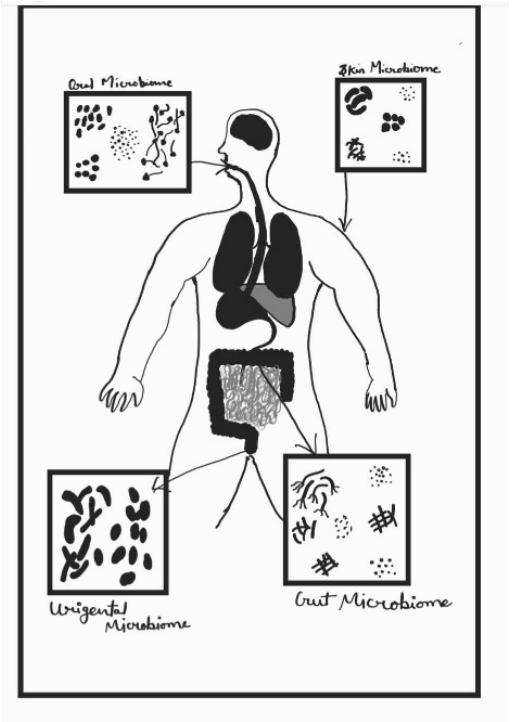

Figure 1: Microbiome found in body areas.

Table 1: Bacteria commonly found in the human colon[8]

S. No.	Bacterium	Incidence (%)
01	Bacteroides fragilis	100
02	Bacteroides melaninogenicus	100
03	Bacteroides oralis	100
04	Enterococcus faecalis	100
05	Escherichia coli	100
06	Enterobacter sp.	40–80
07	Klebsiella sp.	40–80
08	Bifidobacterium bifidum	30–70
09	Staphylococcus aureus	30–50
10	Lactobacillus	20–60
11	Clostridium perfringens	25–35
12	Proteus mirabilis	5–55
13	Clostridium tetani	1–35
14	Clostridium septicum	5–25
15	Pseudomonas aeruginosa	3–11
16	Salmonella enterica	3–7
17	Klebsiella sp.	40-80
18	Enterobacter sp.	40-80
19	Proteus mirabilis	5-55
20	Pseudomonas aeruginosa	3-11

"functional." The epithelial barrier, which consists of enterocytes, Paneth cells that secrete antimicrobial peptides, and goblet cells that secrete mucin, makes up the fourth layer.[6] There are very few types of microorganisms in the stomach and small intestine, whereas the colon has the greatest microbial communities with 10^{12} cells per gramme of intestinal fluid. Since many bacterial species cannot be grown outside of their host's body, they are not well investigated. In the human gut, four major bacterial phyla are primarily present. Actinomycetota, Bacteroidota, Pseudomonodota, and Bacillota. Most bacteria are classified into several genera, including Clostriadium, Peptococcus, Ruminococcus, and Bacteroides, among many others. Roughly 30% of all intestinal bacteria are found in species belonging to the genus Bacteroides alone.[7]

Most bacteria cannot survive in the stomach due to the acidic environment it contains. The three main bacteria found there are Lactobacillus, Streptococcus, and Peptostreptococcus. These are gram-negative spiral bacteria that grow on the stomach mucosa and cause diseases like peptic ulcers and gastritis.[8]

3. Application of Gut Microbiomes

An increasing body of research shows that the trillions of bacteria and archaea that live in the human gut regulate a wide range of metabolisms that are related to host health. These metabolisms include the fermentation and digestion of different biomolecules, the breakdown of xenobiotics and the biotransformation of heavy metals, the production of immune regulators and special metabolites, energy production, epithelial homeostasis, the production of short-chain fatty acids (SCFAs), and many more.[9] Research on the largest community in terms of both abundance and diversity has been the focus of human gut microbial research. Age stabilization was achieved in the past through dietary ingredients and the use of antibiotics. When developing therapies based on the microbiota, it will be crucial to define the ecological principles that control colonization and succession in the microbiota. Furthermore, a significant issue going forward will be developing microbiota-based therapies that are resilient to the wide interpersonal variation and variability of a person's microbiome. Identifying and engineering bacteria that are stable and prominent in the microbiota, as well as putting together cocktails of bacteria that retain a particular function despite changes in the underlying constituent species, are some strategies to address this issue.[10]

3.1. Bioengineering of microbiomes

The primary microbiomes found within the environment can be used to describe it. The interaction that occurs between microorganisms and their hosts, as well as among microbial communities, in response to metabolite production, is what gives ecosystems their distinctive characteristics. As a result, an excessive amount of environmental modification by jumbled microorganisms can disturb soil fertility and lower host fitness. Microbiome engineering can improve the host phenotype and benefit the ecosystem by changing the microbial makeup.[11]

3.2. Human microbiome bioengineering

The Human Microbiome Project (HMP) has advanced to a point where it is possible to study metagenomics characterization of the bacteria found in the human body, namely those found in the gut, oral cavity, lungs, skin, and nasal origin. The knowledge that the HMP gathers will be helpful in the field of microbial engineering to develop ways for reestablishing the balance of microbiota for therapeutic purposes.

3.3. Creating bioengineered microbiomes in plants and animals

Like human microbiomes, animal microbiomes are made up of various microbial communities that are correlated with the growth and well-being of their hosts. Recent research has primarily examined the gut microbiomes of animals such as mice, pigs, cows, rats, and broilers. Despite being the most often utilized, mice and rats make excellent models for the engineering of microorganisms. The most widely used antimicrobial agent is an antibody, which is used to prevent bacterial infections and stimulate animal growth. However, the administration of antibodies led to antibiotic resistance; therefore, feed enzyme probiotics and prebiotics are used in microbiome engineering to change the microbial composition and provide an appropriate antibiotic substitute. Plant microbes are influenced by a variety of factors, including the abiotic environment, microbe-microbe interaction, and host genotype. Root related microbiomes are microbiomes that are present in plants. Plant physiology is the primary function of microbiomes, and their engineering can have anti-pathogenic effects by changing the composition and networking of bacteria to enhance phenotypes like plant growth and fitness.[11]

3.4. Dietary interventions

Dietary fibre from foods like whole grains, resistant starch, and fruits is especially beneficial for the establishment of a diversified microbiome. Dietary fibre plays a crucial role in both health and disease. Patients with IBS have been found to benefit from dietary modifications, with some patients being advised to cut back on their intake of fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs). Because FODMAPs are easily fermented by the microbiome but poorly digested by humans, a low-FODMAPS diet (LFD) offers a way to use nutritional availability to influence the composition of the microbiome. Because creating and maintaining dysbiosis may have long-term health effects, long-term LFD is not advised for people with IBS. A wide range of diets have been studied for their potential benefits in treating Crohn's disease (CD) or ulcerative colitis (UC), two conditions for which dietary treatments have been thoroughly investigated. Among these diets are partial enteral nutrition (PEN), Crohn's disease treatment with eating (CD-TREAT), LFD, Mediterranean diet (MD), exclusive enteral nutrition (EEN), and Crohn's disease exclusion diet (CDED). Out of all these diets, only two—EEN and CDED—have demonstrated clinical success in treating CD and have supporting data about their effects on the GI flora.[12]

According to the suggested mode of action, the GI environment, host immune system, and microbiota are all interacting with inflammatory dietary components. Eliminating these goods will therefore lessen inflammation and the CD symptoms that go along with it. After EEN proved to be successful, CDED was created to let patients consume entire meals while limiting their intake of inflammatory foods, dairy, gluten, and food additives. Bacteria belonging to the Firmicutes phylum are more abundant than those belonging to the Proteobacteria and Actinobacteria phyla, according to both EEN and CDED. Following CDED, there were more bacteria from the Clostridiales class and fewer from the Gammaproteobacteria class; however, changes at the family or species level have not yet been discovered.[12]

3.5. Prebiotics

Numerous dietary fibres function as prebiotics, which are substances found in food that the microbiome uses to support a variety of good bacteria, offer health benefits, and are simple to consume. Prebiotics currently fall into five major classes: Fructooligosaccharides (FOS, GOS, and inulin) and polyunsaturated fatty acids are among the five types of oligosaccharides that are easily fermentable. miscellaneous oligosaccharides include phenolics and phytochemicals, human milk oligosaccharides, and miscellaneous oligosaccharides.[12]

Both FOS and GOS have demonstrated effectiveness in treating GI disorders like IBS as well as metabolic conditions like prediabetes and obesity. Prebiotics have been shown to have adverse effects, including gas, bloating, and diarrhea, even at low dosages. These symptoms may make some of the illnesses being treated worse. Now, babies receive the prebiotics GOS and fructans through infant formula on a regular basis. Prebiotics have been shown to increase the number of lactobacilli and bifidobacteria in the gastrointestinal microbiome, which has been linked to a lower risk of allergic reactions and respiratory infections. Prebiotic-treated patients will have a subset known as "non-responders," much as with previous treatments. The dependency on the patient having microorganisms that can metabolism the medicine may be one factor contributing to patients being "non-responders." Therefore, in comparison to a patient who began treatment with a larger amount of bifidobacteria, the rise in abundance would be lower or nonexistent if the patient had a smaller amount initially. Therefore, interventions that directly introduce healthy bacteria into the gut may improve patient outcomes in

addition to the supply of prebiotics to feed the existing microbiota population. [12]

3.6. Probiotics and symbiotic

Since at least 10,000 years ago, people have been consuming probiotics, which were formerly found in foods like yoghurt and fermented milk. It was discovered that these fermented meals typically had a mixture of lactic acid-producing bacterial strains, such as lactobacilli, bifidobacteria, or other types that can be advantageous under certain conditions. It was discovered that these fermented meals typically had a mixture of lactic acid-producing bacterial strains, such as lactobacilli, bifidobacteria, or other types that can be advantageous under certain conditions. Probiotics can interact with epithelial or dendritic cells to control both innate and adaptive immune responses in the host. These contacts trigger T and B cells as well as macrophages to mount anti-inflammatory immune responses. They may also enhance the synthesis of mucin. [13]

Probiotics typically do not colonize the gut. Therefore, prolonged, or repeated treatment may be necessary to maintain the benefit in cases where efficacy depends on the presence of bacteria. Probiotics may not directly colonize the GI tract, but their fleeting presence seems to facilitate the colonization of other advantageous bacteria, including strains of Clostridium, Blautia, and Lachnoclostridium. Crucially, the probiotic did not colonize these mice. It is hypothesized that either the probiotics interacted with the intestinal epithelium to produce an anti-inflammatory response, or they interacted with the intestinal barrier to strengthen its integrity to produce these positive effects. Probiotics, however, appear to be beneficial for individuals with pouchitis or those who have just finished antibiotic therapy; yet this utility of probiotics in treating pouchitis is still debatable. Symbiotic are treatments that involve the synergistic combination of probiotics and certain prebiotics. There are two subgroups of symbiotic: complementary symbiotic, in which the prebiotic component promotes the growth and survival of other bacteria that are already present in the microbiota and are referred to as autochthonous bacteria, and synergistic symbiotic, in which the prebiotic acts by supplying nutrients for the probiotic. When fructooligosaccharide (FOS) is combined with Bifidobacterium longum, Bifidobacterium breve, or Bifidobacterium bifidum, for instance, the bifidobacteria preferentially metabolize the FOS, which increases the quantity of bacteria. Additionally, the establishment of advantageous cross-feeding networks is made possible by symbiotic combinations. This happens when the probiotic strains break down the symbiotic, and the leftover byproducts can be fed to other helpful bacteria. [13]

3.7. Microbiome mimetics

Microbiota mimetics describes any technique that replicates the interaction between the microbiota and the host, that generates a therapeutically favorable consequence. Fermented infant formulae (FIFs) and paraprobiotics are the two primary kinds of postbiotics. Bacterial proteins and polysaccharides are examples of non-viable components of bacteria that are known as paraprobiotics. FIFs, on the other hand, are the refined byproducts that arise from bacterial fermentation of baby formula. Many microbiome-based medications may already have FDA or other strict regulatory body approval for human use, negating the need for preclinical safety studies. Typical meals that might contain probiotics, postbiotics, or prebiotics are among them, as are other medications that have been repurposed as microbiome mimics. [13]

3.8. Restoration of the microbiota

Numerous treatments have been created and applied to treat illnesses brought on by dysbiosis. There are several approaches to replenish gut microbiota, such as: Treatments involving (a) probiotics, prebiotics, and modified probiotics (b) Faecal Transplanting microbiota (FMT).

4. Probiotic, Prebiotic, and Engineered Probiotic Therapies

The human microbiome has developed into a biomarker in recent years that can indicate a person's health state, offer a prognosis, and forecast how effectively a drug will function. It was projected that food conglomerates, nutraceutical companies, and probiotic production companies would dominate the $46.55 billion worldwide probiotic industry. Probiotic organisms derived mostly from the digestive system or traditionally fermented foods like yoghurt, pickles, and kefir grains are examples of these goods. Therefore, many probiotics used in research and production of probiotics for sale come from a limited number of species, namely the Lactobacillus and Bifidobacterium species. Because probiotics are defined and grown in a pure culture, the danger associated with them is decreased. Probiotics and symbiotics can effectively lower diabetics' fasting blood sugar levels, most likely by reestablishing the disturbed ecology, according to a new meta-analysis. Among the many probiotics that are sold commercially are Lactobacillus species, Bifidobacterium species, Escherichia coli, Enterococci, and Weissella species. [13]

LBPs are defined as symbiotic bacteria identified from the human host based on their utilization in relation to a certain ailment. When it comes to creating products pertaining to the microbiome, most American companies either go down one of two paths: (i) FDA-approved treatments for medical conditions, or (ii) the less rigorous, less expensive route of over-the-counter probiotics that

make claims about their structure and function as well as wellness. [13]

4.1. Faecal microbiota transplantation (FMT)

The microbiota found in the faeces is incredibly diverse, comprising hundreds of types of bacteria. The composition of the microbiome differs between individuals and between individuals throughout time. The microbiota is a dynamic, metabolically active, living organism that is influenced in different ways by diet and other environmental variables. To affect the microbiota of recipients, FMT entails transplanting minimally changed microorganisms from human donors to recipients (including autologous transplantation). By delivering a complete, stable population of bacteria, FMT aims to replace or restore the natural microbiota. FMT has been shown to be an effective therapeutic option for the treatment of Clostridium difficile infection (CDI), a serious illness that results in over 250,000 hospitalizations and 14,000 deaths annually in the United States, in addition to aiding in the restoration of a healthy gut microbiota. Faecal microbiota transplantation is the process of introducing purified faecal microbiota or a faecal solution from a healthy donor into the intestines of a sick patient. It is now the most effective treatment for rCDI and can also be used to treat a wide range of digestive problems such as IBS, food allergies, obesity, diabetes, anorexia nervosa, inflammation of the gut, and neurodegenerative and neurodevelopmental disorders.

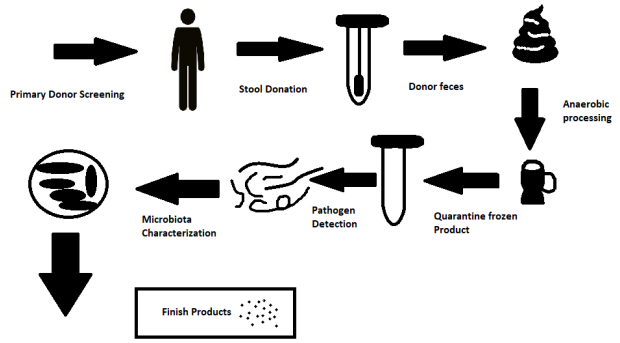

Figure 2: FMT flow chart

FMT is often administered by upper gastrointestinal tract injection, enema, or colonoscopy. From a pre-screened faecal sample, an ecosystem of gut bacteria with structural and functional equilibrium is transplanted. A patient is more prone to acquire a health condition when their gut flora is out of balance. This is often due to antibiotic medication, which eliminates some bacteria while leaving others that are naturally resistant to the drugs to proliferate and overpopulate the gut. The bacterium most frequently associated with this problem is C. difficile. Examples of the large range of products in this category include frozen faeces, freeze-dried stool, and more sophisticated products such capsules containing synthetic stool that is constructed and manufactured in culture. [13]

Factors utilizing the treatment of faecal microbiota transplantation to replenish the microbiome.

4.1.1. Heterologous Source

1. Donation guided by the patient.
2. Universal or stool donor
3. Autologous: supplied by the recipient while the microbiota is still healthy and preserved for later use.

4.1.2. Administration

There are two distinct ways to give medication:

1. Upper gastrointestinal tract
   (a) Endotracheal tubes
   (b) Delivery of Capsules
   (c) By using this method, the number of transmitted microorganisms that tiny intestine immune cells are exposed to is reduced.

2. Gastrointestinal tract in lower

1. (a) An enema for retention
   (b) The sigmoidoscopy
   (c) Colonoscopy
   (d) Large volumes can be delivered using this route and it can be used for direct distribution to be specified locations.

4.1.3. Utilization and results

1. Infection with Clostridium difficile
2. Irritable bowel syndrome
3. Creature resistant to multiple drugs [14]

4.2. Current FMT regulatory environment

4.2.1. United States

The New England Journal of Medicine released the first randomised controlled trial of FMT in 2013 after Dutch researchers found evidence of its use in the US. In May 2013, the FDA hosted a public symposium to discuss the scientific and regulatory issues surrounding FMT. At the workshop, the FDA designated FMT as an unapproved biologic drug. Therapy could only be given in clinical trial settings or in an emergency. Before giving FMT to patients for whatever reason, investigators would need to submit an IND application. [13]

4.2.2. Canada

Compared to the US, Health Canada has stricter and more limited consumption guidelines. The usage guidelines in Health Canada are stricter and more onerous than those in the US. Health Canada specifies a list of viruses and microbiome-mediated diseases for which donors must be

negative, requires doctors to obtain informed permission, and sets standards for recordkeeping. Furthermore, the donor must be known to the patient or a medical professional attending to the patient. Patients with rCDI are limited to undergoing FMT under a CTA in the absence of these requirements. [13]

4.2.3. European Union

Member states now have decision-making authority granted to them by the EMA. At the 2012 European-level group, the Competent Authorities on Substances of Human Origin Expert determined that faeces are not HCT/P and are not eligible for inclusion in the European Human Tissue Directive 2004/23/EC. [13]

4.2.4. Belgium

The stool products used in FMT are seen as components of the human body, like human tissues or cells. The recommendations of the SHC were put into effect by the FAMHP in October 2018, following legislative updates in Belgium in December 2008 that permitted the classification of stool as an HCT/P. [13]

4.2.5. France

The Agency National de Security du Medicament et des Products (ANSM) has FMT on its list of investigational drugs. FMT produced by a hospital or pharmacy is permitted to be used in clinical trials with approval or when produced in accordance with Article L.5121-1 of the French Code of Public Health. When all other therapeutic alternatives have been exhausted and conventional therapies have failed, FMT should be the last resort. [13]

4.2.6. Britain

Medicines and healthcare goods are governed by the Medicines and Healthcare goods Regulation Agency (MHRA). The June 2015 MHRA position document highlights several possibilities for patients to receive FMT. Pharmacies can prepare FMT for patients in three different ways: according to a prescription for a specific patient (referred to as the "magistral option"), for the patients of the pharmacy (referred to as the "official formula"), or through clinical trials. According to the needs of each patient, a doctor may prescribe FMT under the "Specials" framework for usage under close supervision. [13]

4.3. Obesity management

The herbal products had diverse effects on microbial phylum in gut microbiota, although most of the trials showed an increase in the Actinobacteria phylum, as Bifidobacterium spp. enriched after intervention Interventions exerted inconsistent impacts on Firmicutes and Bacteroidetes abundances. Firmicutes were decreased after the intake of Schisandra chinensis or Rehmannia glutinosa extracts, although this phylum showed no changes after Bofutsushosan and Arabinoxylan intakes. On the other hand, an increase in Firmicutes was observed after inulin-type fructans consumption. Alteration of Bacteroidetes was also inconsistent after various interventions. [15]

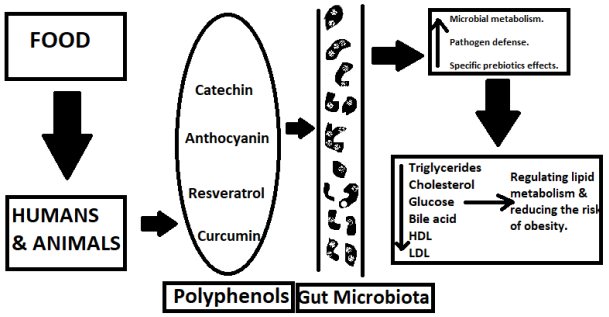

Figure 3: Gut microbiota and their actions.

5. Current Condition of Microbiomes

Microbiome-focused businesses have been funded more frequently and show no signs of stopping off. Attempts to turn these businesses into publicly traded firms have also decreased. For instance, Seres Therapeutics (NASDAQ: MCRB) raised slightly under USD$134 million in a highly publicized initial public offering in the middle of 2015. The financial journals and mainstream media began to cover microbiome startups by the autumn of 2016, after they had been garnering significant financing and attention for some time. An article about the financial elements of the microbiome that was published in September 2016 in the Wall Street Journal is frequently cited. This story confirmed what many had been wondering for a while: more money than ever is being invested in microbiome startups. Over USD $600 million had been invested in enterprises during the first three quarters of 2016, which is more than 400% more than the previous year. The report points out that the amount invested in the first three quarters of 2016 alone—over USD $600 million—is larger than the total amount invested in microbiome startups between 2011 and 2015. [16]

According to estimates, the human microbiome market will be valued at $380 million in 2022 and will expand at a compound annual growth rate (CAGR) of 23.8% during the projected year. Before the Human Microbiome Project (HMP) was launched in 2007, the human microbiome was a largely uncharted territory. The goal of the experiment was to comprehend the idea of the core human microbiome and how it interacts with the host's physiology. Numerous studies pertaining to the microbiome have been carried out because of the notable developments in sequencing and analytical techniques, as well as the 40% rise in non-HMP

investments. The HMP and other studies have produced research discoveries that shed light on the function that gut microbiota plays in regulating an individual's overall health and well-being as well as the etiology of numerous diseases because of changes in the composition of the resident gut microbiota. According to the findings, dysbiosis, or an imbalance of gut bacteria, is specifically linked to the development of several chronic illnesses, such as diabetes, ulcerative colitis, Crohn's disease, and Clostridium difficile infections (CDIs). The human microbiome has gained attention recently due to its links to immunity and several respiratory disorders. It is well recognized that a healthy immune system is linked to the gut microbiome. Lung, pulmonary, and other illnesses have been linked to variations in the number of microorganisms, including actinobacteria, firmicute, and Bacteroidetes, according to research.[17]

There are so many products present on the market at the present time which is made up of microbes and they produce well and effective effects on the human health.

5.1. SERES therapeutics

It is a late clinical stage biotech working on a wide range of diseases through the modulation of human micro biomes; they are designed to modulate the key functions by altering makeup of gut microbiome. This company recently published their data for phase 3 ECOSPOR III study for the prevention of C. difficile.[24]

5.2. Vedanta biosciences

They focus on the gastrointestinal disorder's infectious disease as well as oncology in their pipeline. Vedanta Bioscience recently declared their Phase 2 study results from their lead program, VE303, VE202, VE800. This data includes the study of C. difficile infection.

5.3. Finch therapeutics

They developed therapies that are affected by the patients linked to the distribution on the microbiomes, it recently became the first company that show a microbiome therapy that reach its primary goals in F&D Administration trial for the patients who are infected by C. difficile.[25]

5.4. Prebiotics

They mainly focused on the disease that can be treated by human microbiomes.[26]

6. Conclusion

In conclusion, the document provides a comprehensive overview of the human microbiome and its significance in health and disease. The human microbiome, composed of trillions of microorganisms, plays a vital role in various metabolic processes, immune regulation, energy production, and overall host health. The composition and function of the gut microbiome undergo significant changes during the first year of life and can be influenced by factors such as diet and antibiotics. Research on the human microbiome has focused primarily on understanding its role in health conditions such as liver diseases, diabetes, inflammatory bowel disease, autoimmune diseases, colon cancer, and central nervous system disorders. The document also highlights the different sequencing techniques used in microbiome research and the concept of the halobiont and hollo genome. Furthermore, the document discusses the importance of studying the microbiome in the context of ecosystem health, as a healthy ambient microbiome is essential for maintaining a healthy human microbiome. It also emphasizes the potential applications of microbiome research in bioengineering and dietary interventions, particularly in the development of probiotics and prebiotics. Overall, the document emphasizes the need for further research and understanding of the human microbiome to improve human health and develop innovative therapies for various health conditions.

7. Future Aspects of Microbiomes

Microbiomes in therapeutics have a bright future ahead of them in several medical specialties. The various communities of microbes that reside in and on the human body are known as microbiomes, and they are essential to both preserving and preventing illness. Here are a few prospective future features:

7.1. Precision medicine

Therapeutics based on the microbiome could lead to individualized care. Comprehending the distinct microbiome makeup of an individual may facilitate the development of customized medicines that aim to address microbial imbalances linked to a range of illnesses.

7.2. Disease prevention and treatment

Studies have shown connections between diseases like obesity, autoimmune diseases, mental health problems, and even cancer and microbiota. To prevent or treat these illnesses, future medicines may include modifying or altering the microbiome.

7.3. Drugs based on the microbiome

Probiotics, prebiotics, postbiotics, and live biotherapeutics are examples of microbiome-based medications that are being developed with the goal of modifying, enhancing, or restoring the microbiome for therapeutic purposes. These could be tailored bacteria to target diseases or microbial transplants.

Table 2: Microbiome products

S. No	Product Name	Bacteria Name	Functions
1	Sava Pop to Debloat	B. longum, L. casei, L. rhamnosus, L. acidophilus	Bloating reduction, Rebuilt gut microbiomes [18]
2	Furlicks Gut Health	Bacillus Coagulans 5B CFU	Improve digestion enhance immune system [19]
3	The Good Bug Metabolically Lean	Loctobacillus cosel, 400million CFU, Loctobacillus rhamnosus 400million CFU, Streptococcus ehermophilus 400 million CFU	Boost metabolism, help manage weight, improve energy level [20]
4	The Good Bug Gut Balance	Loctobacillus rhamnosus GG 3 billion CFU	Improve immunity and digestion [21]
5	Wow Probiotics	L. Plantarum, L. fermentum, L. acidophilus, B. infantis, L. casei	Improve digestion and immunity [19]
6	Fossence Probiotic Dietary Fiber	Loctobacclius and Bifidobacteria	Improve immunity [22]
7	Wellbeing Nutrition Melt into a Healthy Gut	Bacillus Coagulansm 10 billion CFU	Reduce gastric acidity and bloating [23]
8	Healthy Hey	Probiotics 50 billion CFU, L. acidophilus, L. rhamnosus, L. plantarum, L. paracasei, Saccharomyces boulardii	Balance intestinal ecology, Promote healthy digestion

7.4. Therapies based on the gut-brain axis

The gut-brain axis links brain activity and mental well-being to the gut flora. Therapeutic approaches that focus on this axis may result in new ways to treat diseases like anxiety, depression, autism, and neurodegenerative illnesses.

7.5. Immune system modulation

Research on the microbiome points to its function in immune system training and modulation. Treatments that target the microbiome may be able to improve the effectiveness of immunotherapies or aid in the management of autoimmune illnesses.

7.6. Fighting antibiotic resistance

The creation of treatments based on the microbiome may provide an alternative to conventional antibiotics. By supporting a healthy microbiome, these medicines may strengthen the body's natural defense mechanisms instead of directly targeting bacteria, potentially lowering the need for antibiotics.

7.7. Diagnostic tools

Developing a better understanding of the microbiome's function in health and illness may result in the creation of diagnostic tools. These could include tracking treatment responses or using microbiome profiling to detect diseases early.

7.8. Regulatory challenges

To guarantee the safety, effectiveness, and standardized production of microbiome-based therapeutics, regulatory frameworks will need to change as these treatments continue to develop.

8. Source of Funding

None.

9. Conflict of Interest

None.

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