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Gut Microbiota in Human Metabolic Health and Disease

Elike.Mounika[1],Gadi.Alekhya[2], Yerraguntla Blandina.Manjulatha[2], Pennada.Bindu DeviPriya[3],Pichikala.Likhitha[3],Polavarapu.Maniteja[3]

1. B.Pharm/Sri Vasavi Institute of Pharmaceutical Sciences/Andhra University/India

1. B.Pharm/Sri Vasavi Institute of Pharmaceutical Sciences/Andhra University/India

2. Professor/Department of Pharmaceutical Bio Technology/Sri Vasavi Institute of Pharmaceutical Sciences/ Andhra University/India

3. B.Pharm/Sri Vasavi Institute of Pharmaceutical Sciences/Andhra University/India

3.B.Pharm/Sri Vasavi Institute of Pharmaceutical Sciences/Andhra University/India

3.B.Pharm/Sri Vasavi Institute of Pharmaceutical Sciences/Andhra University/India

Abstract

In the last fifteen years, studies have demonstrated a connection between alterations in gut microbiota and a number of illnesses, including cancer, diabetes, obesity, liver, and neurological conditions. The emergency of innovative medicines has been facilitated by this underscoring the significance of comprehending the functions of gut microorganisms in managing many health concerns. The gut is home to about 1000 different species of bacteria, and its core microbiome has more than 6000 functional gene groups. The host immune system and metabolism are controlled by gut microorganisms. The amount of microbiome sequencing data has grown dramatically in the last ten years, and this information is vital for both diagnosing and treating immune system, inflammatory, and colonic diseases. Microbiota represents a next-generation medicinal tool for innovative therapeutic actions, as some strains may impact the course of cancer and the effectiveness of treatments, improving precision medicine in diagnosis and treatment. A varied population of bacteria in the human gastrointestinal system known as gut microbiome interact with the host in both directions and is impacted by environmental, lifestyles, and developmental factors.

Keywords: Microbiota; Diseases; Methods; Advantages; Disadvantages Functions;; Therapeutic Applications; Limitations.

I. Introduction

Over the past ten years, there has been a notable increase in knowledge and interest in the gut microbiota. [1] The microbiome that exists in humans is made up of bacteria, viruses, archaea, and eukaryotic microorganisms. This compound has a major impact on immune system education, metabolism, and infection defense. [2] The group of bacteria known as the human microbiota is crucial to immunity, digestion, detoxification, immune system development, and overall health. Age, diet, illness, and two inherited genomes all have an impact on the acquired microbiota that makes up the microbiome. [3] The pathophysiology of intestinal illnesses such as obesity, cardiovascular disease, and inflammatory bowel disease is significantly influenced by the gut microbiota. Therefore, comprehending microbiome activity is crucial for creating future Tailored healthcare plans and may also offer novel medication development target. [4]A diet consists of macro- and micro-nutrients, providing energy and structural strength. Macro-nutrients like carbohydrates, protein, and fat provide energy, while micro-nutrients like vitamins, minerals, and bioactive compounds regulate biochemical processes and protect against diseases. Antioxidants, such as antioxidant molecules, have health-promoting benefits against free radicals. [5]

II. IMPORTANCE OF GUT MICROBIOMES FOR HUMAN HEAITH

2.1Prebiotic interactions with the microbiome

Dietary prebiotics are fermented ingredients that alter the gastrointestinal microbiota, providing health benefits. However, the definition has been debated due to the need for selective metabolism. A consensus statement revised the definition to "a substrate used by host microorganisms for health benefits, " but still requires a selective microbiota-mediated mechanism for prebiotics to be defined. [6]

2.2Microbiome Nutrition Interaction Between Diseased Gut

The gut microbiota plays a major influence in medication metabolism, dietary calorific bioavailability, obesity, IBD, autism, immune system conditioning, and post-surgical recovery, according to high-throughput genomic sequencing technology. [7]

III. LINK BETWEEN GUT MICROBIOME AND HEALTH

3.1Cancer

Gut dysbiosis, infections, and antimicrobial medication use are some of the variables that can increase the risk of colorectal cancer. Gastric and extraintestinal malignancies may be influenced by gut microbiome. Fusobacterium and Clostridium are overrepresented in gastric cancer patients. Environmental and host factors influence breast cancer progression, but bacterial communities also play a role. [8] Through imaging, sequencing, cultivation methods, and genetically modified mice models, recent research raises questions regarding the existence, metabolic activity, and functional significance of intratumoral microbiota in cancer. [9] There have been major developments in understanding the elements that determine how a tumor responds to cancer therapy. The main variables affecting how well a patient responds to cancer treatment have been tumor-centric indicators, tumor metabolism, and immunological sensitivity to effectors. On the other hand, indicators today provide a comprehensive paradigm by encompassing a wide range of attributes. [10]

3.2Gut microbiome transplantation on kidney

Research indicates that the gut microbiota and certain circumstances affect the transplantation of solid organs and hematopoietic stem cells, resulting in a reduction of microbial diversity after transplant. Kidney transplantation doesn't involve gut mucosa or drainage, but gut microbiota changes may impact outcomes. However, studies show a correlation, not a causal link . This review summarizes in vivo and clinical evidence on gut microbiota effects on kidney transplantation. [11]

3.3Inflammatory bowel disease

The immune system problems that underlie IBD, such as Crohn's disease and ulcerative colitis, are influenced by the microbiome, genetics, and risk factors. This has led to the development of medicines that modify the microbiome. [12]

3.3.1 Ulcerative colitis

Severe morbidity is a common occurrence in adults and children suffering with ulcerative colitis (UC), a chronic inflammation of the colon. Despite the lack of complete understanding of the pathophysiology, it is necessary to develop new therapeutic approaches. The immune system is triggered by the etiology of ulcerative colitis (UC), which upsets the host-microbe equilibrium. There is a genetic inclination in people whose susceptibility loci are associated with handling of microbes. The distal bowel location of the disease raises the possibility that bacteria are involved as wellModels of murine colitis demonstrate that alterations in the gut microbiota and the return of bacteria result in a decrease in inflammation. The inflammation that was earlier decreased by diverting the fecal stream returns when humans are exposed to fecal effluent again. [13]

3.3.2Crohn's disease

IBD, sometimes referred to as ulcerative colitis (UC), is a disorder marked by inflammation in the ileum and other digestive system regions. Compared to CD, UC is more genetically predisposed and linked to autoimmune disorders. Moreover, twin concordance and increased inheritance rates are linked to it. Evidence suggests that bacteria or the gut microbiota may be involved in the pathophysiology of CD. Clinical symptoms can be alleviated by prolonged antibiotic courses, exposure to luminal contents, and fecal stream diversion. Animals devoid of germs do not develop IBD, and granulomas in the intestinal wall could be an indication of an immunological response to bacteria or their byproducts. [14]

3.4Cardiovascular disease

According to recent research, the onset and progression of cardiovascular illnesses are greatly influenced by the gut microbiome and its metabolites. It is possible that the makeup of the gut microbiota is influenced by the oral microbiome, which could further exacerbate these disorders. [15] High rates of morbidity and death are associated with cardiovascular diseases (CVDs), and risk factors for CVDs include smoking, obesity, diabetes, poor diet, and high cholesterol.

According to recent studies, the development and progression of cardiovascular disease are significantly influenced by the gut microbiota and its metabolites. The composition of the gut and oral microbiota can affect disease, but it can be adjusted by boosting community structure with probiotics and prebiotics. [16]

3.5Rheumatoid Arthritis

About 0.5% to 1.0% of people have rheumatoid arthritis (RA), a chronic inflammatory illness that destroys joints and impairs function. Autoantibodies and weakened immune systems are part of its pathogenesis, and genetic predisposition also plays a role. The chance of getting RA is further increased by environmental factors such as host microbiota, alcohol, smoking , birth weight, food, and geography. It is well recognized that smoking raises the risk. A key factor in the onset and course of RA is the gut microbiome. [17]

3.6Chronic Liver Disease

Eighty percent of the body's macrophages are found in the liver, which is also in charge of eliminating food items and germs from the gut. Additionally, it controls immunological reactions, which encourages T-cell tolerance. Changes in the composition of the gut microbiota may impact homeostatic mechanisms and result in liver disease and hepatic dysfunction. [18]

3.7 Immune System Disorders

3.7.1Autoimmune Diseases

In genetically predisposed individuals, environmental variables lead to autoimmune diseases (AID), with epigenetic dysregulation being a contributing factor. The pathophysiology of AID is influenced by environmental factors such as pesticides, smoking, and heavy metals. The gut microbiome, in particular dysbiosis, induces pro-inflammatory and immune-deregulatory responses that lead to autoimmune diseases . Antigen-presenting cells (APCs) sample antigens and trigger an inflammatory milieu to start autoimmune disease states. Pathogenic autoimmune pro-inflammatory reactions, including Th17 activation, can result from modifications in the profiles of the gut microbiota. [`19] A compromised immune system is the main cause of autoimmune illnesses, which impact 24 million people in the US and disproportionately affect women. The impact of environmental factors in autoimmune illnesses, such as nutrition and composition of the gut microbiome, is being explored. [20]

3.7.2Allergies and Inflammatory Conditions

Research has shown that the microbiota has a major role in the rise in the incidence of allergic illnesses, such as food and respiratory allergies, in recent decades. The innate and acquired immune systems, as well as cellular development, organ and tissue creation, and immune response modulation are all influenced by the microbiome. The "hygiene-hypothesis" postulates that modifications to the skin, gut, or lung microbiome due to dysbiosis result in altered composition and metabolic activity. It has not been demonstrated that the idea, with an emphasis on personal hygiene, is valid for independent host variables. [21]

IV. METHODS FOR STUDYING OF GUT MICROBIOMES

4.1 Next-generation sequencing techniques

4.1.1.16S rRNA Sequencing techniques

It is difficult to sequence specimens with distinct nucleic acids, particularly in microbiota, because the Sanger technique requires pure DNA and yields only one episode. [22] Targeted sequencing of particular genes, such the 16S rRNA gene, makes studying the microbiome simple and affordable. In a single PCR reaction, universal primers may both amplify and identify bacteria. However, the PCR methodology may skew the results, the approach may be biased, and the correctness of the reference database determines how reads are assigned . [23]

4.1.2.Shotgun metagenomics

Direct sequencing of ambient genetic material, or metagenomics, has revealed previously undiscovered species and provided new understanding of entire microbial communities. Researchers investigate microbiologically varied ecosystems such as soil, marine water, and the gut through thousands of metagenomic initiatives. Particular taxonomic combinations of genes and genomes, which compose metabolism, define these ecosystems. Because microbial cells make up the human genome, genomic studies can identify genes linked to antibiotic resistance or enzyme synthesis, highlighting the critical role that microbiota plays in human health. [24]

4.2.Metabolomic pathways in the gut

The gut microbiota is an important factor that influences the potential health impacts of functional meals by influencing digestion, xenobiotic transformation, and micronutrient delivery. Additionally influencing gut microbiota growth and metabolism can have an impact on the makeup and possible roles of these microorganisms in food. While tannins are broken down by microbial enzymes to produce conjugated derivatives with various pharmacological profiles, tea phenolics have the ability to suppress some species of gut bacteria. Few research, however, have looked into how food supplements, such as animal-based versus plant-based diets and more Bifidobacterium species in breastfed infants, impact the metabolism of the gut microbiota. To fully comprehend these interconnections, more investigation is required. [25]

V. FUNCTIONS OF GUT MICROBIOMES

5.1. Nutrient metabolism

Nutritional genetic and epigenetic variables all impact the human gut microbiota, which is essential for nutritional metabolism. This microbiome's messengers, metabolites, affect how the gut microbiota interacts with the host. It is essential to comprehend these relationships and alter microbial ecology in order to create therapeutic interventions that effectively treat disorders associated with nutrition. [26]

5.1.1.Fermentation of dietary fibers

The hundreds of bacteria strains that make up the human gut microbiota are essential to health because they inhibit colonization and boost the immune system. But dysbiosis can also result in obesity, cancer, inflammation, and cardiovascular disease. Because of their chemical structures and interactions, dietary fibers improve health outcomes and support a healthy colonic microbiome. To find the dietary fibers that enhance the formation of SCFA and support beneficial species, studies have been carried out. [27]

5.2 Immune system modulation

This study investigates the dual mechanisms by which nutrition influences immunity directly through altering immune cells, and indirectly through influencing the microbiota or nonimmune organs. It addresses undernutrition and malnutrition in low-to-middle-income environments as well as overnutrition in high-income countries when examining how nutrition affects immune-mediated diseases. Additionally, the study looks at how different foods affect immune responses, offering mechanistic insights into how different cells interact. [28]

5.2.1.Gut Associated Iymphoid Tissue

With over 40 trillion microorganisms, the human gut microbiota is diverse and offers several important health benefits, including metabolite production, detoxification, and colonization avoidance. Intestinal pathologies such as Crohn's disease, ulcerative colitis, and inflammatory bowel diseases (IBD) can be caused by pathogens, thus the intestinal immune system has to react to these bacteria and maintain active protection against them. The largest diversity and quantity of immune cells and compartments, such as effector sites and gut-associated lymphoid tissues (GALT), are found in the colon. Because it is difficult to get human intestinal tissue and there are no established techniques for collection and analysis, our current understanding of human GALT is limited.[29]

5.3.Protection Against Pathogens

5.3.1.The gut microbiota's functions in pathogen defense

Recent research reveals the non-immune and immune-mediated processes, as well as the methods by which commensal bacteria impart infection resistance. These strategies can be either indirect pathways or direct generation of inhibitory molecules. The review focuses on systemic immunity, the protective role of intestinal microbiota against gastrointestinal bacterial pathogens, and innovative therapeutic techniques that employ commensal microbes and their products to treat infections. [30]

5.3.2.Immunological disorders, inflammatory reactions, and pathogen colonization are all strongly impacted by the gut microbiota

Symbiotic bacteria boost immune responses, prevent pathogen colonization, and preserve immune homeostasis through mechanisms including resource competition and direct killingInfection and inflammatory illnesses are more likely to occur when the gut microbiota is altered by genetic and environmental factors. It is essential to comprehend this connection for the treatment and prevention of disease. [31]

VI. THERAPEUTIC APPLICATIONS

6.1.Probiotic and prebiotics in different diseases

Chronic illnesses such as colorectal cancer and IBD have been reported to respond better to probiotic treatment. Probiotic therapy can control the inflammatory response. Inflammation in the gut microbiome is a characteristic of IBD. [32]A major concern to world health is cardiovascular disorders, which include thromboembolic disease, arrhythmia, venous thrombosis, hypertensive heart disease, cardiomyopathy, and coronary artery disease. Cardiovascular illnesses were the cause of 18 million fatalities in 2015, or 12.5% of deaths from all causes. One important risk factor for heart attacks and strokes is atherosclerosis, a long-term inflammatory condition driven by fat. Genetics, a bad lifestyle, and hypertension are risk factors. Metabolic dysregulation, which raises cholesterol and damages blood vessels and causes atherosclerosis, is frequently linked to hypertension. [33]Gastrointestinal (GI) malignancies continue to be a major worldwide health concern despite therapeutic advances. They make up 25% of all cancers and 9% of all cancer-related deaths. 500,000 new instances of oesophageal cancer were reported in 2005, The most frequent type is the most common. Gastric cancer is the second most common cause of cancer-related deaths worldwide and has the second-highest incidence rate. Small intestine neoplasms are uncommon, and colorectal cancer is the third most common type of cancer globally. Studies on colorectal cancer (CRC) and stomach and esophageal cancers highlight the potential cancer-preventive/therapeutic benefits of microbiota in GI malignancies. When taken, probiotics have health benefits. [34]

6.2. Role of gut microbes in diseases and their potential therapeutic applications

6.2.1.Cardiovascular disease

Globally cardiovascular diseases (CVDs), which are impacted by both environmental and hereditary factors, are the primary causes of morbidity and mortality. A complex community of interacting organisms, the gut microbiome may play

roles in CVDs, as recent investigations have shown. Unbalances in the gut microbiota can affect a person's susceptibility to thrombosis, obesity, insulin resistance, atherosclerosis, and immunological response, all of which can raise their risk of cardiovascular disease. There is discussion of therapeutic approaches to alter gut microorganisms. [35]

6.2.2. Cancer

A number of variables including lifestyle choices, genetic predisposition, and exposure to the environment, contribute to cancer's status as the second greatest cause of death globally. A diverse community of commensal bacteria known as the gut microbiota is important for maintaining health including and preventing pathologic disorders like cancer. Comprising bacteria, fungi, viruses, and archaea, the gut microbiota is essential for vitamin synthesis, nutrition metabolism, and defense against gut pathogens. Dysbiosis, a disorder connected to a number of human diseases, cancer, can result from an imbalance in this balance. The impact of specific bacterial species on human health can now be better understood because to recent developments in metagenomics and transcriptomics. Studies have linked the gut microbiota to tumorigenesis, a frequent disease that has a dual role in preventing cancer. [36]

6.2.3. Inflammatory bowel disease

In genetically predisposed hosts, inflammatory bowel diseases (IBD) are chronic inflammatory disorders brought on by an improper immune response to gut microorganisms. Since the turn of the 20th century, the incidence has gone up in industrialized countries but is still rising in emerging countries. IBD is caused by a number of factors, including host genetics, immunological responses, gut flora, and environmental stressors. The importance of the microbiome in the development of IBD has been made clear by high-throughput deep sequencing technologies, which has also improved our understanding of the functional mechanisms involved. [37]

6.2.4.Gut –Liver axis

The relationship between the gut and liver, which is impacted by nutritional, genetic, and environmental variables, is known as the gut-liver axis. It is connected to dysbiosis of the microbiota, intestinal barrier function, and immunological response. The gut barrier and the gut microbiota are both greatly impacted by bile. Since dysbiosis of the intestinal microbiota is associated with liver disorders such as NASH, HE, cirrhosis, ALD, and NAFLD, the liver plays a critical role in regulating the intestinal flora itself. Prebiotics, probiotics, symbiotics, antibiotics, and FMT are examples of future treatments. [38]

VII. CHALLENGES AND CONSIDERATIONS

Our knowledge of the human body has greatly increased as a result of scientific research and awareness of the human microbiome, a continually expanding community of bacteria within human organisms. Our concept of normalcy, sickness, and ourselves will all be profoundly altered by this research, which will also have a profound impact on public health initiatives, clinical practice, and the creation and marketing of commercial goods. Concerns regarding possible abuse and misuse are raised by the growing use of fetal microbiota transplantation (FMT). Although its precise significance is still up for debate, the microbiome has a profound impact on both health and illness. Although there has been progress in research, the human microbiome is still frequently portrayed in social media as novel or alluring. Frequently, the general population applies this science to health decisions without taking long-term hazards into account. Changing a person's microbiome to improve their health has ethical ramifications rather than being viewed as a technical or medical problem. [39]

VIII. FUTURE DIRECTIONS IN GUT MICROBIOME RESEARCH

The study of the human gut microbiome, which is essential to comprehending health and disease, is a result of the Human Genome Project, which was finished ten years ago. The most diverse and numerous microbial population, with substantial host-microbe interactions, is found in the gut. From descriptive surveys to high-definition descriptions of composition, function, and ecology, current methodologies have evolved. Success requires cooperation between microbiologists, molecular biologists, computational scientists, and bioinformatics specialists in addition to doctors. Determining the gut microbiome's impact on gastrointestinal and nutritional disorders requires an understanding of healthy human gut microbiomes. Since the development of molecular tools, complex interdependence among gut bacteria has supplanted cultivation-based methods as the primary means of understanding the human gut microbiome. [40]

8.1.The role of microbiomes in personalized medicine

IBD, diabetes, cirrhosis, and colorectal cancer have all been related to dysregulation of the microbiota-host relationship. Research indicates that the effectiveness of drugs depends on the interactions between immune systems and microorganisms.

Combinations of gut microbiomes can influence how well cancer patients respond to treatment. A biomarker for illness phenotype, prognosis, and therapy response is the gut microbiome. It is linked to increased mucosa-associated F.prausnitzii and surgery for celiac disease. Other gastrointestinal disorders, such C.difficile infection, are linked to microbiome characteristics that can forecast illness. Prevotella has been confirmed in rheumatoid arthritis patients by recent research that found gut microbial signatures in these patients. [41]

IX. ADVANTAGES AND DISADVANTAGES

9.1.Metagenomicsexamining the high -resolution profiling of the gut

Microbiota and characterizing the gene architecture of uncultivated microbiota through sequencing data, information on the microbiota's functional contributions, and information not required for the cloning of particular genes. The gut microbiota does not produce it's own functions.

9.2.Metatranscriptomics

Sensitivity of RNA/DNA sequencing for high resolution gene expression profiling and differentional Expression of microbial genes in diverse physiological and environmental conditions high sensitivity,high throughput,quantitative technique,gut microbiota characterization[both known and unknown],and assessment of microbial interaction low microbial mRNA stability,a lack of a specific procedure, unknown typical samples and the requirements for numerous purification stages.[42]

X. LIMITATIONS/RESTRAINT

Microbiota-based metabolic illness models fail in global applications, highlighting the importance of localized baseline and disease models for predicting metabolic risks. [43] The present method for detecting uncultured microbiota is based on baxonomic data and complicated bioinformatic analysis, which can be costly and time-consuming. [44] The main focus of the study is the bottom-up investigation of the relationship between gut microbiota and depression-related brain chemistry and behavior. The gut's makeup effects emotion, cognition, and brain functioning. However, there is limited evidence that the brain has a top-down influence on the microbiome. The brain's management of gastrointestinal motility, secretory activity, immunological responses, and psychological stress can all influence microbiome composition, although the direct brain signaling influence on the microbiome is unknown. [45]

XI. Conclusion

A wide variety of microorganisms, such as bacteria, viruses, fungus, and archaea, are found in our stomachs. Although there has been progress in identifying new bacteria and examining the composition of the microbiota, investigations have shown variances under various circumstances. To comprehend the function of gut microbiota in the pathophysiology of CVD and to create innovative diagnostic and treatment approaches, more research is required. The movement towards actionable ''gut health.'' Which is founded on evidence-based microbiome science,promotes lifestyle choice including exercise,stree reduction,probiotics,and nutrition for their potential to improve microbiome-related health.

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