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Gut Microbiome and Human Health- A Brief Overview

Ashraf Navab Moghal. B. E[1], Manjunatha. K[1], Nithin. B[1], Sri Charan. A[1], Usama Zaid. J[1], Suman. P[2]
[1]*PG Students, Department of Microbiology, Nrupathunga University, Government Science College, Bangalore-01, India*
[2]*Assistant Professor, Department of Microbiology, Nrupathunga University, Government Science College, Bangalore-01, India*

Abstract: ***Humans have co-evolved with microorganisms, which play a pivotal role in determining the overall well-being of biological systems. Evolution has made certain species of bacteria thrive in the human gut, utilising the catabolized nutrients of the host and exhibiting symbiosis. It chiefly comprises a densely populated group of microbes, collectively called the Gut Microbiota. The relationship between the human system and the gut microbiome is a very sparsely introduced subject yet managed to catch everyone's eye, just for its sheer complexity. The nature and type of microbe present in the gut vary widely with respect to socio-economic, ethnic, and geographic influences. There has been extensive study done and some are underway showcasing the potential link between the gut-microbiome and the host, humans. As amusing as the gut-microbiome it is, its relationship with the host is quite remarkable. The gut-human connection is important in metabolism, coordination (brain axis), immunity, and, of course, disease. The diseases that were known earlier have recently been known to be associated with the gut microflora. Hence, this area of gut and human health has been in the focus of researchers and scientists in recent times. In this review literature, we have tried to consolidate the health aspects of humans influenced by gut dysbiosis. A few interactions are also discussed, like metabolic activity, gut-brain axis, drug action, diet influence, and immunity. This literature is aimed at showcasing the association and complexity of the gut microbiome with human health.***
Keywords: Gut microbiome, Diseases, Central nervous system, Obesity, Diabetes, Cardiovascular system.

I. INTRODUCTION

Human health defines the proper functioning of all the biological systems within our body. These vital systems include the CNS, CVS (cardiovascular system), immune system, digestive system, respiratory system, and so on. Numerous factors influence the overall well-being of our health. These factors include the levels of hormones, glucose levels, neurotransmitters released in the brain, levels of antibodies released during an infection, the amount of oxygen occupied in the lungs during inhalation, and so on. The biological systems have to coordinate and cooperate with each other to maintain the overall integrity of the body. From time immemorial, microflora has been residing in our gut, but its impact and significance is a topic which has been overlooked till date. Recent studies have shown that the gut microbiome influences various vital bodily processes that contribute to the overall wellbeing of human health. Now, what is this gut microbiome? As simple as the word seems, the gut microbiome defines the variety of microorganisms, mainly bacteria, present in our gut. Bacteria are primitive prokaryotic unicellular microorganisms that are known to be found in a wide range of habitats, from freezing polar regions to thermal hot-springs to deep ocean oil dwells.

Although the size of the bacterium is small, the impact it has on humans' overall health is colossal. These tiny dudes reside in our gut and multiply by utilising the nutrients ingested via food. The influence of these minuscule is due to the metabolites which are released during and after their metabolic processes. Certain types of bacteria are known to breakdown complex fatty acids and other compounds and make them freely available for absorption through the blood. Gut bacteria are host-friendly, which means no harm to the host. But sometimes, due to certain unprecedented genetic mutations, these microbiome members turn evil and sabotage the gut integrity, which leads to a variety of gut diseases, which lead to a variety of gut diseases collectively called inflammatory bowel disorders. Any research in any discipline of science is carried out in order to improve the standards of human health and well-being. Thus, the prime focus of every research undertaken is finding new and effective possibilities to fight diseases, overcome ageing discover vaccines, and other human-oriented inventions. Human health can be described as the proper functioning of physical and mental processes. The physical processes include all the muscle movements, whereas the mental processes define the cognitive abilities and other brain-related activities such as memory, verbal skills, comprehension skills, etc.

There are myriad factors that influence human health. These factors can be both intrinsic as well as extrinsic. Extrinsic factors include socio-economic status, culture, and region of residence, whereas intrinsic factors are attributed to the biochemical processes occurring inside the body.

Each and every biochemical process occurring within the body is vital for maintaining its integrity. Movement of muscles, firing of neurons in the brain, formation of memories, defense against infections, pumping of blood, respiration, biosynthesis of proteins, nucleic acids and fatty acids ,breakdown of the same to yield energy and many more are of paramount importance and vital for the healthy survival of an individual. There are a number of factors which influence the proper functioning of the aforementioned processes, among which the gut microbiome is becoming a prominent factor. As described in the introduction, the gut microbiome is attributed to the diverse microorganisms predominantly colonized by bacteria residing in our gut. The metabolites of gut microbiome origin greatly influence the overall integrity of the body. The following paragraphs describe the influence of the gut microbiome on various biological systems and its significance:

II. GUT MICROBIOME AND CENTRAL NERVOUS SYSTEM:

The central nervous system, abbreviated as CNS, is the most important system which controls the functioning of all other systems in our body. It comprises the brain and spinal cord. Even though the brain occupies only a small portion with respect to the body's mass, the energy consumed by it is a mind-boggling 20% of total produced energy.

Proper functioning of this vital muscular organ is significant for thinking, comprehending, deciding, feeling, memorizing, and performing work. A small impairment in its function can lead to myriad disorders. One of the many factors that influence brain health is the gut microbiome.

The whole of human body is protected against deadly infections by a well organized group of special cells which together form our immune system. Likewise, brain to have special cells called astrocytes which prevent inflammation by inducing T cell Apoptosis through TRAIL DRS signaling *(Sanmarco et al., 2021).* TRAIL is a protein and expression of this inducer protein is driven by interferon IFN, produced by meningeal natural killer cells.

In turn, the expression of IFN he is modulated by the gut microbiome. the metabolites produced from the gut microbiome interfere with the synthetic pathways of various vital processes there by either enhancing or any beating the effect of hippocampus is complex brain structure deeply embedded in the temporal lobe known as memory site. It processes and stores long term and short term memories.

As it's work is a consistent one the energy required for the process two is a normal get microbiota is known to influence the metabolic coupling between astrocytes and neurons which is an essential process for generation of energy for brain functioning, it is found that the expression of the six gene deals vital for the astrocytes lactic shuttle is influenced by the different varieties of bacteria present in the gut microbiome. This influence is proved by an experiment, where in divers get of a mice was colonized with diverse microbiota for 24 hours and expression of essential genes ATP1A2 and PFKFB3 showed significant enhancement *(Chen et al., 2017).*

III. HUMORAL IMMUNITY AND GUT MICROBIOME:

The host immune effector that controls the microbiota and prevents mucosal infection is IgA Gut microbiota-derived factors include molecular pattern recognition receptor ligands and nutrient-derived metabolites such as short chain fatty acids and adenosine triphosphate, as well as host-derived factors such as retinoic acid, various cytokines and cytokine-like molecules. Gut microbiota-derived factors induce B cell responses, activation, and differentiation *(Lazar et al., 2018).*

The gut microbiota provides important health benefits to the host, such as enhanced energy harvest from diet and activation of the immune system. The gut microbiota also ensures a mutually beneficial microbial symbiosis with the host. The mucosal antibody IGA is important in regulating the host immune system because the microbiota produces a myriad of cellular constituents and metabolites which promote the population and maturation of immune cells in gut-associated lymphoid tissues *(Kim & Kim et al., 2017).* As a result, the host and gut microbes produce and use short-chain fatty acids (SCFA's) to produce bile acids and vitamin B12 to maintain nutritional, physiologic, and immunological homeostasis.

IV. THE EFFECTS OF THE GUT MICROBIOME ON GASTRO-INTESTINAL TRACT

1) *Digestive System*: Millions of microorganisms enter our body through our diet *(Bull & Plummer, 2014).* Our gut hosts a plethora of microorganisms since it has all the necessary factors like nutrients, temperature, pH, water activity, etc., to facilitate effective growth of them. The diversity of gut microflora is influenced by the diet we follow. Recent research has proven that the gut microbiome significantly impacts mood and mental behavior *(Xu & Gordon, 2003*) & *(Bull & Plummer, 2014).* (Mood-affecting chemicals like serotonin are produced in large amounts in the gut.)

2) *Mouth*: It is the place where food, along with microbes, enters the digestive system. According to research at present, a healthy man consists of 100 to 200 species of living microbes. Whichever is most harmless, it actively protects us from infection. Accumulation of these microbes in large scale causes tooth decay, acrid breath, and other diseases, so cleaning the tongue and mouth on a regular basis is mandatory to protect ourselves from unwelcoming infections. *Helicobacter pylori* is a bacteria and is the predominant bacterial species in the mouth *(Bäckhed et al., 2005).* An increase in their number can lead to the formation of mouth ulcers, which can totally impede your talking ability. Washing your mouth with glycerin is one of the best measures to prevent this painful condition. Recent studies have shown that *Helicobacter pylori* plays a significant role in maintaining human gut health. It modulates the immune system. Reduce your chances of infection, allergies, and asthma. It prevents esophageal cancer and gastric reflux disease. It helps to regulate appetite (*Nicholson et al., 2012*). Experiment evidence shows that removing this bacteria from the mouth causes weight gain (experimental evidence).
3) *The digestive tract*: Bacteria in our body convert the undigested compounds into useful chemicals which can be further absorbed by the body. *Lactobacillus* is present in trillions in the stomach, which maintains the pH of the gut and ensures its survival for its counterparts *(Neish, 2009)*. The gut hosts a plethora of microbes, collectively referred to as the gut microbiome, which play a significant role in maintaining the overall health of a human being *(Thursby & Juge, 2017).*
4) *Diet*: An old saying goes, "you are what you eat," which holds true for the gut microbiome. People who eat healthy food have a more diverse microbiome compared to others, improving their overall wellbeing. What makes a good microbiome? There are trillions of microorganisms of which bacteria occupy the upper hand in the then gut microbiome composition. There has been extensive research on the topic of gut microbiomes around the world, and while no firm conclusion has been reached, it has been proven that diversity in gut microbiomes is attributed to an individual's improvement in health. Studies of health-promoting probiotic species are yielding biological insights that might promote drug development *(Bengmark, 1998).* Diseases like cancer and autoimmune disorders are thought to be influenced by processes in the gut microbiome, which includes multiple sclerosis and autism spectrum disorders *(Bull & Plummer, 2014).* The gut is where the drugs we intake are digested and processed, leading to strong interactions between them, and these minuscule influence the gut-drug interactions too. There is also evidence that proves the influence of the gut microbiome on mental health and cognition. There is a growing public interest in gut microbiome research, which frequently focuses on personal dietary choices *(Rowland et al., 2017).*

V. DISORDERS OF THE GUT

A. *Irritable Bowel Syndrome (IBD)*

The disease IBD has been addressed as a global phenomenon wherein it's estimated 3.5 million people are diagnosed with having IBD irrespective of its types *(Kaplan G, 2015)*. IBD is basically a lesion or inflammation of the mucosal lining of the gut, occurring mainly because of a dysregulated immune system, resulting in gut dysbiosis.

Crohn's disease (CD), Ulcerative Disorder (UD), and Inflammatory Bowel Syndrome (IBS) are known for causing chronic inflammatory diseases *(Kaser et al., 2010)*. The disorder has been seen across various countries, which is discussed in detail regarding the demographics for the prevalence of IBD *(Kaplan, G., & Ng, 2017).* The influence of this disease is not clearly understood, but rather studies show it to be related to host-genetic and some environmental factors. Association analyses identify 38 susceptibility loci for inflammatory bowel disease and highlight shared genetic risk across populations *(Liu et al., 2015*). Recent advances also hint towards pathogenesis causing these disturbances by some pathogens and decreasing certain other groups of commensal microbes *(Takahashi et al., 2016)* & *(Wills et al., 2014).*

In Crohn's Disease, *Bacteroides, Eubacterium, Faecalibacterium*, and *Ruminococcus* are reduced. In particular, *Akkermansia muciniphila* and *Faecalibacterium prausnitz*i are the most extensively studied bacteria in CD *(Fukuda & Fujita, 2014).*

F. Prausnitzii and *Escherichia coli* in 28 healthy controls, 45 CD patients, 28 UC patients, and 10 IBS patients. They found that *F. Prausnitzii* is a predictor of "health" in patients with CD (and other gut disorders*). F. Prausnitzii* abundance was decreased in CD patients and it was lower than in patients with IBS and healthy controls. When E. coli was added to *F. Prausnitzii* in the diagnostic analysis, it discriminated the ileo-colonic vs. colonic form of CD patients. The combination of certain bacterial groups might improve the diagnostic value of gut microbiota analysis *(Fukuda et al., 2014).* A need to find biomarkers for identifying this disease is yet challenging. The influence of IBD across various age groups, drug influence, resistivity, diet and many such unanswered questions are left behind by quality tests and studies across various environments is needed.

Recent findings reflect that not only bacteria but also fungi like Candida species are opportunistic microorganisms, and their pathogenic role might be immune stimulation after mucosal barrier dysfunction. Also, in IBD patients, a genetic mutation against fungi (e.g., DECTIN-1 and Card9) may increase fungal colonisation and subsequent inflammation (Richard et al., 2015).

Virus: Most of the human gut virome is composed of bacteriophages. 68 human gut bacteriophage trials in IBD showed consistent results. Although there is a paucity of trials, most of them indicate an increased abundance of *Caudovirales* and a decreased *virome* diversity *(Richard et al., 2015)* & *(Wagner et al., 2013).* Although gut parasites and protozoa are mostly accepted as pathogenic microorganisms, there is evidence that parasites can shift mucosal immune response in IBD *(Croese, J, 2006).*
Blastocystis species and *Dientamoeba fragilis* are found in human feces, and they infect humans by the fecal-oral route *(Garcia, 2016)* & *(Wawrzyniak et al., 2013).* A recent trial also found that *Blastocystis* species are associated with healthy (increased diversity) gut microbiota *(Brands et al., 2019).* Both *Blastocystis* and *D. fragilis* were lower in active UD; however, they are elevated in remission and healthy controls *(Tito et al., 2018).*

B. Obesity And Gut Microbiota

Obesity is a major global health problem which is caused by hereditary and environmental factors. It is a mutual relationship between the host and an intestinal microorganism *(Liu et al., 2021).* The gut contains more than a trillion organisms. Some of these microorganisms are like *Methanobacteriales, Christenseneliaceae, Lactobacillus,* and *Bifidobacteria (Castaner et al., 2018).*
According to the world health organisation, whose BMI is greater than 30 is said to be obese. It varies from country to country. Obesity is also related to diseases like cardiovascular disease, diabetes, and cancer. The mucus secretion by the gut and dead cells serves as their nutrients and increases their population in the gut. The *Firmicutes* and *Bacteroides* are dominant in the gut. They undergo degradation of polysaccharides and lipopolysaccharides, Lipoprotein lipase (LPL), production of short-chain fatty acids (SCFA), vitamins and amino acids *(Zhang et al., 2009)* & *(Shreiner et al., 2015).*

1) *The Major Role of gut Microbes in Obesity:* The first obvious is to degrade the foods which are not digested by human beings, like fermentation of dietary fibers, which results in the production of short-chain fatty acids (SCFA). This SCFA can induce lipogenisis and, by molecular pathway, increase the storage of triglycerides. Another relationship is studied in germ-free mice, which were transplanted with the gut microbiota of conventionally bred mice. This procedure resulted in the development of insulin resistance and increased fat content in germ free mice. By using 16s rRNA gene sequencing, we found evidence for obesity in these mice (Davis, 2016). The dominant phyla *firmicutes* and *bacteroides* are found to be true in humans as well. Similar evidence was later found to be true in humans as well. The gut microbiota is seen as more efficient in obese people compared to skinny people. Because of the energy from dietary fiber and fat storage. Obese people have a higher amount of SCFA and reduced residual food calories in their stool than skinny people. There is still a knowledge gap regarding the role of gut microbiota in obesity.
2) *Gut Microbiota Modification:* Diet has a significant impact on gut modification. A slight change in diet profile can increase the number of *Bacteroidetes* in the gut microbiota within 24 hours; for example, a person fed high fat content food can increase the number of *Bacteroidetes* within 24 hours. Diets high in fat and low in fiber can increase the number of *Bacteroidetes* while decreasing the number of plant polysaccharide degrading microorganisms like *Ruminococcus bromii (Arumugam et al., 2011).*

C. Gut Microbiome and Diabetes

Diabetes has become a global phenomenon, rapidly growing and has been enlisted as the deadliest disease. According to the IDF's 2021 survey, approximately 537 million adults (20-80) worldwide are diabetic.3 in 1 adult is for diabetics inhabiting low and middle income countries (Sun et al., 2022). Diabetes has caused 6.7 million deaths. The data related to Type 1 Diabetes (T1D) is also equally alarming, wherein 1.2 million children and adolescents suffer from this autoimmune disorder. 541 million people are suspected to develop Type 2 Diabetes (T2D). Type 1 Diabetes is the major disorder when compared to T1D, which stands at 10.
A country such as India, with its burden of malnutrition and standard of living, is facing a problem in handling this metabolic disorder *(Sharma & Tripathi, 2019).* Even the rich country's original western/modern lifestyle includes an incidence of this disorder *(Mehta et al., 2009).* T1D, as previously known, can occur by means of inheritance, lifestyle, and environmental factors. So, why the stomach?... It's been observed that gut dysbiosis is associated with diabetes and obesity *(Xu et al., 2016).* There's a significant change going on in the gut microflora's composition. *Acidophilus, L. amylovorus,* and others were found to be less than usual *(Forslund et al., 2015*). T2D and obesity share the inflammatory component in tissues relating to metabolism regulation, such as the liver, adipose, and muscles *(Pickup & Crook, 1998).* This inflammation is caused by dysbiosis, which is characterised by an excess of cytokines, interleukin (IL6 & 1), TNF-a. This causes stress in the insulin signal and results in diabetes *(Hotamisligil, G. 2006).* Studies revealed that T2D Subjects had a lower number of *clostridiales* which were known to produce useful SCFA *(Qin et al., 2012).* Significant changes are also seen in the intestinal flora *(Larsen et al., 2010)* & *(Qin et al., 2012).*

1) *T1D (Type 1 Diabetes):* This disorder occurs in infants and is characterised as an autoimmune disorder because the T-cell causes annihilation of the insulin-producing beta cells in the pancreas. The gut composition of g+ anaerobes (*Lachnospiraceae & Ruminococcaceae*) is more predominant after period of Breastfeeding *(Dominguez et al., 2010), (Koenig J et al., 2010)* & *(Palmer et al., 2007).* The healthy subjects had more balanced microbiota, predominantly *butyrate-producing sp. Bacteriodetes*, gut permeability is also an important factor related to fermentation of SCFA, determining the level of permeability *(Brown et al., 2011), (Van Immerseel et al., 2010).* Butyrate's role as an anti-inflammatory is exemplary in the case of T1D, which is less and distorted *(Sokol et al., 2008).* Through current studies, much evidence has been established for the treatment for T1D and T2D diabetes. Therapeutics based on diet as prebiotics Probiotics and certain chemotherapeutics (Metfromin) *(Wu et al., 2017).* Extensive studies in the field of diet-based approaches need to be conducted in order to control this disorder.

D. Hypersensitivity and the Gut

SCFA metabolites like acetate, butyrate, and propionate possess metabolite-sensing G-protein coupled receptors such as GPR43, GPR41, and GPR109A. These receptors play a determining role in gut dysbiosis, which ultimately leads to an inflammatory response. SCFA's are end products of digesting fiber by commensal bacteria. Hence, if dysbiosis occurs, it affects the formation of SCFA's. Hence, the role of maintaining gut health is of prime importance *(McKenzie et al., 2017).*

Respiratory and food allergies are characterised by a response produced by T lymphocytes producing IL-4, IL-5, IL-13N, and a low production of IFN-(TH-2) by some main effector T cells *(Akdis, 2016).*

These T cells induce subsequent induction of other effector cells, leading to inflammation, such as mast cells, basophils, and eosinophils. Patients with such allergies have become more common in recent decades *(Akinbami et al., 2016) (Prescott et al., 2013),* and all of these cases are linked to gut microbiota *(Blaser & Falkow, 2009)* & *(Trompette et al., 2014).* There is established evidence that the gut microbiome has a central role in allergenicity. They are known to tweak the immune response during organ and tissue formation by both interactions of innate and acquired immune systems *(Palm et al., 2015).*

The geographical or nutritional changes have contributed to gut dysbiosis in the skin, gut, or lungs, causing compositional change and metabolic activity (Hygiene hypothesis) *(Strachan D, 1989).* Earlier childhood infections are associated with less diverse microbiota and could explain the prevalence of atopic disease *(Ege et al., 2011).* The amount of bacteria present is equal to the total number of cells in a human. They contribute to the gene pool of humans, increasing it by 200 times *(Turnbaugh et al., 2007).* As a result, the composition of the gut microbiome is important in the context of human health.

E. Allergies and Food

Excessive immune response is linked to gut dysbiosis, which leads to asthma and atopy diseases. Regulatory T cells carry antigens influenced by dietary factors *(Kim et al., 2016).* Dysbiosis alters the mucosal lining and disrupts immunological norms, resulting in asthma and food allergies *(Aitoro et al., 2017).* There are extensive studies done to mitigate the allergic responses, which predominantly focus on the diet of an individual.

F. Autism and the Gut

Autism Spectrum Disorder (ASD) is a severe neurological disorder during the developmental stages of an infant. This causes a child to socialize less. Children with ASD are frequently correlated with gut dysbiosis (Yang et al., 2018). This causes the gut-brain axis to be disrupted and leads to behavioural change in the children. Interestingly, there is evidence that a probiotic and diet-based approach to ASD has helped in mitigating the behavioral manifestation in children *(Davies et al., 2021).*

G. Cardiovascular Diseases

In many developing and underdeveloped countries, cardiovascular disease is the leading cause of mortality. As per 2018, 17.7 million deaths per year are related to Cardiovascular Disease (CVD) *(Baenjamin et al., 2018) (Shimokawa et al., 2015).* More often, the gut metabolite TMAO (Trimethylamine-N-oxide) is known to occur in the event of CVD and is widely noticed. There is a 2.5-fold increase in TMAO levels in individuals with heart ailments *(Suzuki et l., 2017)* & *(Fu et al., 2016).* Other significant gut metabolites are Indoxyl sulphate and Tryptophanases. This IS reacts in the liver and results in pro-inflammatory and pro-oxidant in cardio mycocetes and cardiac fibroblasts (Huć et al., 2018) & (Kimura et al., 2011). These affect the BP or arteries. The intestinal bacterial fermentation of dietary fiber results in the production of short-chain fatty acids (SCFA'), which make up a sizeable component of the daily energy requirement. Intestinal tract immunological modulation and the development of regulatory T cells are both significantly influenced by SCFA's, particularly butyrate and propionate (Ohira et al., 2017).

The increased acetate generation by rodents' gut bacteria activates the parasympathetic neural system, which encourages hyperphagia, increased insulin release in response to glucose, and obesity (Ohira et al., 2017). The direct effect of SCFA's on the occurrence and progression of cardiovascular illnesses, however, has not been described in any research.

When compared to non-CAD patients with coronary risk factors like diabetes, hypertension, or dyslipidemia and healthy volunteers, patients with CAD have lower levels of the phylum *Bacteroidetes* and higher levels of the order *Lactobacillales.* This was discovered using terminal restriction fragment length polymorphism analysis, one of the most dependable and well-established 16S rRNA-based techniques. When compared to non-CAD controls, the *Firmicutes/ Bacteroidetes* ratio, a sign of dysbiosis, rose in the CAD patients. Interestingly, our results showed that CAD patients were considerably more likely than non-CAD controls to be classified as enterotype, which is distinguished by low levels of *Bacteroides.* A metagenome-wide association analysis of faecal samples from 218 patients with CAD and 187 healthy Chinese people (Jie et al., 2017).

The gut barrier, which has numerous levels and is made up of innate and adaptive immune cells, mucus, epithelial cells, and gut microbiota, plays a significant role in both health and illness. Bacteria can't access the circulatory system through the gut barrier, and abnormalities have been linked to gastrointestinal disorders such as celiac disease, inflammatory bowel disease, and colon cancer, as well as chronic liver disease, type 1 diabetes, obesity, and food allergies. Patients with periodontal disease may have bacteria in their atherosclerotic human plaque. Some atherosclerotic plaque bacterial species, however, are only identified in faeces and cannot be found in the mouth, indicating that gut microbes may possibly contribute to the diversity of atherosclerotic plaque microbial species *(Yin et al., 2015).*

1) *Sulfate of P-cresyl:* Patients with Heart Failure [HF] had significantly greater levels of P-Cresyl Sulphate (PCS), which indicates an increased risk of death or re-hospitalization due to HF *(Wang et al., 2016).* PCS is a metabolite of tyrosine that originates from the gut microbiota. It is processed by at least four different enzymes in four steps, with the first step through the third step occurring in the gut microbes to produce intermediates such as 4-hydroxyphenylpyruvate, 4-hydroxyphenylacetate, and p-cresol, and the fourth and final step occurring in the gut mucosa or liver to produce PCS *(Gryp et al., 2017).* In senior hemodialysis patients, PCS predicts cardiovascular events and all-cause death *(Lin et al., 2013).* Similar to indoxyl sulphate, PCS stimulates NADPH oxidase activity and reactive oxygen species generation, which contribute to direct cytotoxicity to cardiomyocytes, facilitates cardiac death, and causes diastolic dysfunction *(Han et al., 2015).*
2) *Phenylacetylglutamine*: In patients lacking carbamyl phosphate synthetase, phenylacetylglutamine (PAG), which is excreted as a nitrogen waste, can take the role of urea *(Brusilow et al., 1991).* A significant nitrogenous metabolite that builds up in uremia is PAG (Zimmerman et al., 1989). It is a co-metabolite of phenylalanine produced by the host and gut microbes. The conversion of phenylalanine to phenylacetic acid and the activation of phenylacetic acid to create phenylacetyl-CoA and ligate to glutamine are processes carried out in the liver and kidney in humans by aminotransferase and pyruvate ferredoxin oxidoreductase, A (PORA) in bacteria. Aminotransferase and are expressed by Clostridium sporogenes. High serum PAG levels are linked to overall mortality and CVD in those with chronic renal disease *(Dodd et al., 2017) (Moldave et al., 1957)* & *(Poesen et al 2016).* More metabolites generated from the gut microbiota were listed in reference, but it is unclear if they play a role in the pathogenesis of CVD.

VI. CONCLUSION

With all the detailed description about how the gut microbiome influences the vital body process we have been enlightened about its significance and impact on our health and day to day activities. The more diverse the gut micro flora, the more healthy an individual. Gut Microbiome can be literally considered as the second brain of our body.

Serotonin, dopamine, melatonin, epinephrine and many other paramount chemicals predominantly produced in the gut. According to a study, 90% of the seritonin is produced in the gut alone. This significantly shows as the intent with a healthy got influences our mood, decision making etc., With all these importance or we concerned about the second brains health are saying goes we are what we eat and that's true to the fat that the dietary plan we follow tremendously influences the habitat of the gut microbiome. Since there are diversified microorganisms colonizing our gut, the diet we follow should necessarily contain everything from proteins to fat to fibers. Consumption of any of these components is vital yet needs to be in balanced. An imbalanced direct would endangered the gut micro flora and cause a cascading effect to the health of an individual. Moreover the revival of once lost variety is very difficult and sometimes impossible. Thus, the consumption of proper diet and exercise have a significant effect in maintaining the gut environment.

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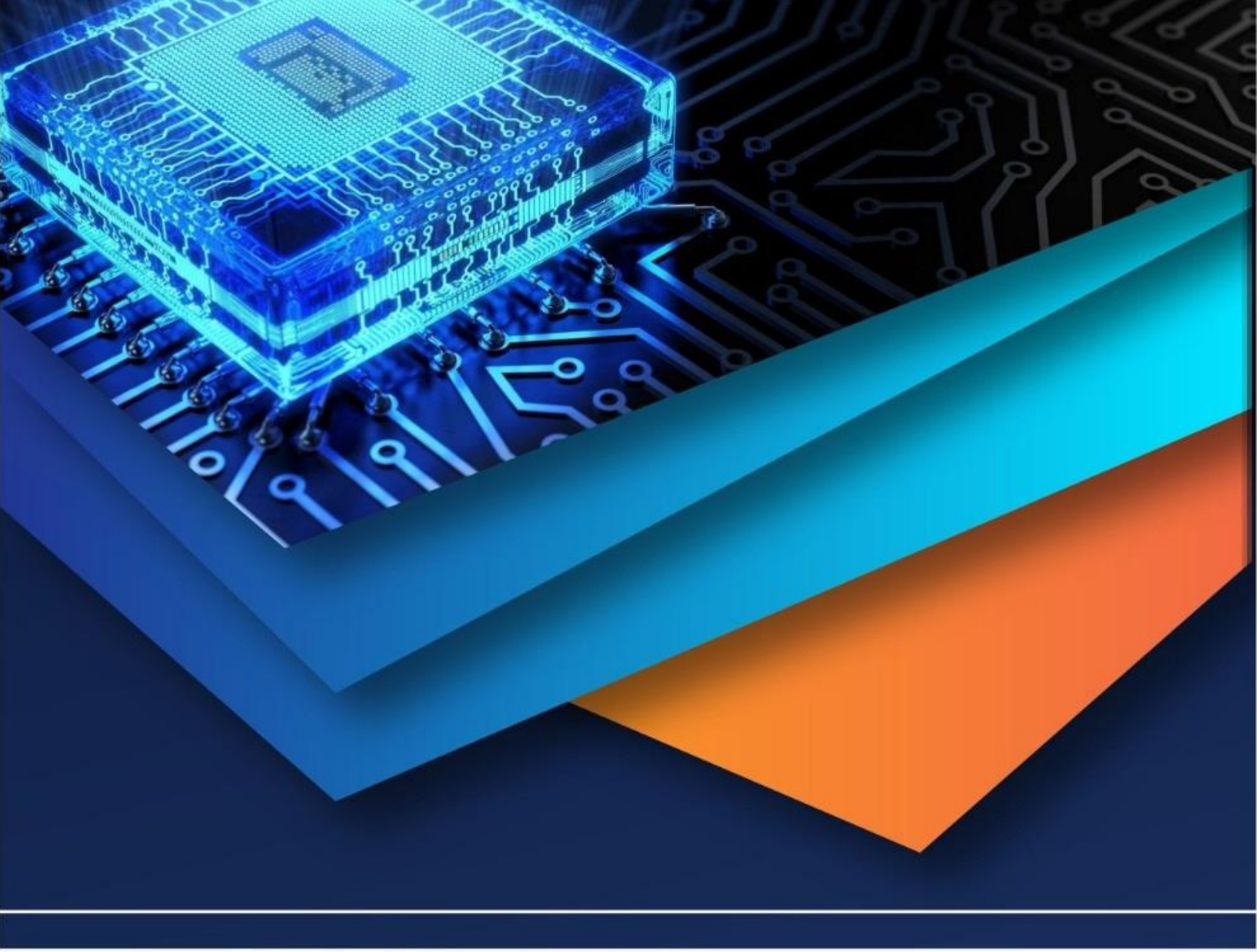

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