



CONCEPT OF HUMAN BRAIN-GUT MICROBIOTA – AN *AYURVEDA* AND MODERN PERSPECTIVE

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ABSTRACT

Ayurveda is a holistic science aimed to maintain health and treat the diseased. In recent years, research has emphasized the role of gut microbiota in human health and metabolic processes. The concept of *Sahaj Krimi* (non-pathogenic microbes) has been described in *Ayurveda* and can be correlated with gut microbiota. The function of gut microbiota depends upon the status of *Agni* (digestive fire). The digestive system has long been an area of critical importance within the *Ayurvedic* system and is only now being acknowledged by modern science as a key component in the regulation of physical and mental well-being. We now recognize that virtually every aspect of our physiology and health is influenced by the collection of microorganisms that live in various parts of our body, especially the gut microbiome. There are many external factors that influence the composition of the gut microbiome but one of the most important is diet and digestion.

Keywords – *Ayurveda*, *Pittadhara Kala*, Brain-Gut microbiota, Gut microbiota.

INTRODUCTION

The human gut microbiota is rich in diverse microbes like bacteria, archaea, and eukaryote colonizing the entire Gastro Intestinal Tract and the genes encoded by these resident bacteria constitutes the microbiome. It comprises trillions of microbes relentlessly attuned to create a complex repertoire of biochemical mechanisms for an adaptively specific ecosystem. It is an inextricable and resilient part of human metabolism,¹ Nutrition,² Immune mechanism³, and mental well-being⁴. *Ayurveda* has an epistemological and theoretical foundation of the Indian medical system, which originated in India. The concept of *Agni* in *Ayurveda* denotes any physiological principle which governs or mediates all the transformation processes in an organism. Almost all functions related to the body and disease causation in *Ayurveda* literature and practice are better revealed through an explanation of physiology and this confines upon the core concept of *Agni* or gastrointestinal and metabolic homeostasis.⁵

PITTADHARA KALA

According to *Ayurveda Dosha*, *Dhatu* and *Mala* are the basic pillars of life. Three doshas help in the physiological function of the body by influencing seven *dhatu*s, *dhatu*s help in the formation and maintenance of the human physical structure, in this process three major by-products formed called *Mala*. *Jatharagni* provides the energy required to keep these physiological activities in harmony.⁶ *Jatharagni* is located in the *Pitta Dosha* and regulates all the *Dhatu*⁷ hence the efficiency of *dhatu*s depends on *Jatharagni*. *Jatharagni* is located in *Pitta* which is secreted during *Dwitiya-Avasthapaak* in *Pittadhara Kala*. *Pittadhara Kala* is situated between *Aamashaya* and *Pakvashaya* also called *Grahani*.⁸ According to *Panchbhautika Chikitsa*, there are 2 types of *Pittas*, *Amla-Pitta*, and *Kshar-Pitta*. For digestion to take place *Amlapitta* and *Ksharpitta* has to be mixed up causing *Madhuryta* which protects other *dhatu*s from getting digested, also explained by *Charak* as “*Ksharo hi Laati Madhuryam Amlopsamhitam.*”⁹ It helps in the development of *Medha* (intelligence), digestion, appetite and satiety, vision, courage, generating heat, and hunger.¹⁰ Hence the development of *Majjadhatu* depends on *Pittadhara Kala*. *Pitta* is secreted as the *mala* (excretory product) of *Rakta*.¹¹ *Rakta* along with *Rasa* nourishes all the *dhatu* including *Majja*. *Majjadhatu* is one of the seven *dhatu*s, whose basic function is *Asthipurana*, which can be correlated as bone marrow fills up the long bone cavity and becomes the major site of RBC production and blood formation.¹² *Pittadhara Kala* helps in *Grahanati*, *Pachati*, *Vivechayati*, *Munchati* with the help of *Saman Vayu*¹³ resides near *Agni*, and may lead to the absorption of elements required in blood formation. When compared *Pittadhara Kala* can be correlated with the lining membrane of the small intestine which plays a vital role in digestion and absorption of all nutritive substances such as Vitamin B12, folate, and iron which are the main source of development and maturation of RBCs.

WHAT DOES THE GUT MICROBIOTA DO?

The gut microbiota provides essential capacities for the fermentation of non-digestible substrates like dietary fibers and endogenous intestinal mucus. This fermentation supports the growth of specialist microbes that produce short-chain fatty acids (SCFAs) and gases.¹⁴ The major SCFAs produced are acetate, propionate, and butyrate. Butyrate is the main energy source for human colonocytes, can induce apoptosis of colon cancer cells, and can activate intestinal gluconeogenesis, having beneficial effects on glucose and energy homeostasis.¹⁵ Butyrate is essential for epithelial cells to consume large amounts of oxygen through β oxidation, generating a state of hypoxia that maintains oxygen balance in the gut, preventing gut microbiota dysbiosis.¹⁶

The gut microbiome participates in vital processes including digestion, energy homeostasis and metabolism, the synthesis of vitamins and other nutrients, and the development and regulation of immune function. It also contributes to the production of numerous compounds that enter the blood and affect various tissues and organs of the body¹⁷. An important consideration is the recognition of the enormous variation in the gut microbiota composition in each individual, as well as in each area of the digestive tract. Throughout the intestines, there are specific niches that house individual microbial communities, which can be

immunologically more active than others. A balanced and diverse microbiome is critical for maintaining health and immunological balance.¹⁸

When the microbiome is in balance it contributes to many health benefits, but when out of balance, it can cause problems in the gut and other areas of the body. Dysbiosis arises when the delicate and elaborate ecology of microbial communities is disrupted by internal or external factors. A disrupted microbiome is characterized by the overgrowth of one or more of the different microbial colonies. A complex interaction between the microbiome and immune systems may result in an inflammatory state¹⁹. An imbalanced microbiome has been associated with a number of gastrointestinal diseases including irritable bowel syndrome (IBS) and inflammatory bowel disorder (IBD)²⁰. Conditions such as asthma, atopy, childhood obesity, and autism spectrum have been correlated with excess antibiotic use and a resulting alteration in the microbiome in childhood²¹. Numerous other conditions such as obesity, autoimmune disorders, cardiovascular disease, cancer, and neurological disorders have also been linked with changes in the microbiome.²²

The gut microbiome also affects the brain and mental health. The basis for this interaction is the gut–brain axis, which consists of the brain, immune system, endocrine system, enteric nervous system (ENS), enteroendocrine system (EEC), and the gut bacteria. There is a bidirectional flow of information between the gut and the brain. The most direct is through the vagus nerve, which is an important and long nerve in the body that regulates many internal functions. A less direct means of communication is through different chemical messengers, such as neurotransmitters, hormones, and peptides.

The gut produces numerous peptides and neurotransmitters. Many of these are also found in the brain. The secretion of these gut-derived chemicals can be influenced by the composition of the gut microbiome. In addition, the gut microbiome can also produce its own unique array of chemical messengers, that go into the bloodstream and affect different parts of the body. There is also research showing that gut microbes can activate immune cells in the gut wall, which causes the release of proinflammatory cytokines and ultimately may affect the permeability of the blood–brain barrier²³. Animal studies have shown that a disrupted microbiome can cause anxiety-like and depression-like behaviors²⁴.

A new field of psychobiotics has even emerged, which utilizes probiotics to affect moods and behavior in humans²⁵. While the precise manner in which the microbiome participates in these many disease states is still not completely clear, there are currently a number of therapeutic approaches that are now being tested in clinical trials including diet, prebiotics, probiotics, antibiotics, and fecal microbiome transplantation (FMT)²⁶. Recent studies, for example, have utilized personalized nutritional advice based on microbiome data and other factors²⁷.

BRAIN-GUT MICROBIOTA AXIS

With human evolution, microbes in the human gut also evolved metabolically. This co-evolution led to a symbiotic gut microbiota that communicates with the brain, the brain-gut microbiota. Around 10^{14} microbes (bacteria, viruses, fungi, and protozoa) are scattered around the throat, skin, and gut, i.e., 10-fold of entire human cells.²⁸ Bacteria belonging to phyla: Firmicutes, and Bacteroides form the most abundant of all 1000 species of brain-gut microbiota.²⁹ Gut microbiota is found between the small intestine to the descending colon,

most abundant in the proximal colon. Wherever most abundant, their species are more diverse and mucosa thicker. Normal gut flora has more anaerobic bacteria than aerobic. Gut microbiota are established at birth and diversify throughout life affected by external factors such as medication, diet, and lifestyle.³⁰ The looped, bidirectional communication between the brain and Gut microbiota uses three signaling mechanisms; viz., nervous, endocrine, and immune systems.³¹ Microbes secrete 5-HT serotonin, short-chain fatty acid (SCFA), interleukin-1, and leptin into the blood which influences cognitive and limbic functions. The brain in turn controls myenteric nerve plexuses indirectly through the parasympathetic nervous system (vagus nerve). This controls intestinal secretions, motility, transit time, permeability, and local endocrine influences.³² Derangement in Brain gut microbiota affects both gut (irritable bowel syndrome) and brain (schizophrenia, Alzheimer's disease, autism, and depression-anxiety). Such malfunction is precipitated by stress, cortisol, age, and antibiotic.³³ Since these communications are yet to be understood completely and hold potential for functional disease therapeutics, we chose to review the Brain gut microbiota axis.

AYURVEDA AND BRAIN-GUT MICROBIOTA CORRELATION

Pittadhara Kala and microbiota function

Pittadhara Kala is the site *Jatharagni* helps in *Dhatuposhan* i. e nourishment and development of *Dhatu*s. *Oja* (immunity), *Bala* (physical and mental strength), *Swasthya* (absence of disease), *Utsah* (energetic), *Sharir-Vridhhi* (physical development), *Aayu* (longevity), *Varna-Prabha* (complexion), *Agni* (digestion) is the function of the *Pittadhara Kala* related *Jatharagni*. When compared with the Gut, *Jatharagni* has a similar function in modulating immunity, the nervous system, metabolism, and the endocrine system.

Bidirectional nature of Pittadhara Kala-Majjadhara Kala and brain-gut microbiota Axis

Acharya Sushrut while discussing the prognosis of snakebite, explained the interdependency and bidirectional relation of *Pittadhara Kala* and *Majjadhara Kala*. BGM Axis is also found to be bidirectional and mutualistic. Hence, we can utilize this gateway to reach any of these systems by influencing the other one.

Purusham Purusham Vivakshet, Prakruti, and different compositions of microbiota influencing brain

Ayurveda believes that each individual is different. To consider individuals for assessment, one needs to specify the state of the patient based on factors such as *Agni* (digestion), *Kostha* (consistency of stool), *Prakruti*, etc. Hence, generalizing the disease is of hindrance in treatment. Brain gut microbiota follows the same idea that the composition of Gut microbiota is different in different individuals and depends on factors such as medicine, diet, lifestyle, stress, etc. The Gut microbiota stabilizes at the time of birth and is under the constant influence of the factors mentioned which is similar to *Prakruti* mentioned in *Ayurveda*. Hence, patients suffering from Brain or *Majja Disorders* need to evaluate realizing the concept of uniqueness.

***Pittadhara Kala* and location of gut microbiota**

Pittadhara Kala lies between *Amashay* and *Pakvashay* whereas the most active part of Gut microbiota all over the intestine connection lies between the small and large intestine due to high substrate availability and site for Bile acid function. The process of digestion requires chyme coming from *Aamashay* to mix with *Ksharipitta* (alkaline salt) excreted in *Pittadahara Kala* for digestion is similar to bile acid function.

Prakriti and Gut Bacteria

One study has examined the relationship between *Prakriti* and the composition of the microbiome. The researchers found that three main *Prakriti* types, *Vata*, *Pitta*, or *Kapha*, had a unique microbiome composition³⁴. The population studied was from the same region and had similar dietary habits. The main bacteria of all the subjects were from the phyla Bacteroidetes and Firmicutes. There were distinct differences between the *Vata*, *Pitta*, or *Kapha* groups in less common bacteria. The extreme *Pitta* individuals, for example, had more butyrate-producing microbes which might help protect them from inflammatory diseases. The extreme *Kapha* women had larger amounts of a type of bacteria called *Prevotella copri*, which has been associated with patients who have rheumatoid arthritis and insulin resistance.

CONCLUSION

With the advancements made in clinical research, the human microbiome in the gut virtually explains the functions and mechanisms, from a microbiological point of view. In *Ayurveda* literature, the concept of *Agni* in its functional and morbid states goes hand in hand with the microbiological concept of the Human Gut Microbiome. We are living in a transitional moment in medicine. New studies are emerging that will help us make better choices. The field of integrative medicine represents an important achievement since it combines the best of modern medicine with the best of traditional systems of natural health, such as *Ayurveda*. Integrative medicine benefits greatly from research on the microbiome because it helps us better understand the ancient practices of *Ayurveda* in the light of modern science.

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