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A CRITICAL REVIEW OF HEALTHY AND DISEASED GUT MICROBIOTA IN ACCORDANCE WITH MODERN SCIENCE AND AYURVEDA

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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. Thus, understanding the complex interactions between diet, gut microbiota, and the host is crucial in the prevention and treatment of chronic diseases that plague our society. The concept of *Sahaj krimi* (nonpathogenic microbes) has been described in the Ayurveda and can be correlated with the 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. Ayurveda resides upon the doctrine of the holistic approach. Study designs that explore the Ayurvedic *Prakriti* (body constitution), *Vikriti* (pathological Conditions) and treatment modalities regarding gut Microbiota will help to offer excellent options for the healthy living of human beings. A critical review has been done on *Pôrakrit* (normal) and *vikrit* (pathological) aspects of gut microbiota in accordance with Ayurveda and modern science.

Keywords: Modern science, gut microbiota, Ayurveda, Diseased gut, *Agni*.

INTRODUCTION

In recent years, research has emphasized the role of gut microbiota in human health and metabolic processes. Thus, understanding the complex interactions between diet, gut microbiota, and the host is crucial in the prevention and treatment of chronic diseases that plague our society. 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. Ayurveda resides upon the doctrine of a holistic approach. Study designs that explore the Ayurvedic *prakriti*, *vikriti*, and treatment modalities regarding gut Microbiota will help to offer excellent options for the healthy living of human beings. A critical review has been done on *prakrit* (normal) and *vikrit*(abnormal) aspects of gut microbiota in accordance with Ayurveda and modern science.

Gut microbiota in Health: Modern perspective

The importance of healthy gut microbiota is not confined to the GIT itself. A number of extraintestinal processes and organ systems are regulated by it.

- **Barrier fortifications and regenerative capacity-** Gut microbiota provides its host with a physical barrier to incoming pathogens by competitive exclusion, such as the occupation of attachment sites, consumption of nutrient sources, and production of antimicrobial substances. It also stimulates the host to produce various antimicrobial compounds[1].
- **Peristalsis and surface maturation-** The identities of microbes/microbial molecules (gut flora) are responsible for the postnatal growth of the intestinal surface area development[2].
- **Nutrition and Metabolism-** A large proportion of the microbiota metabolic processes beneficial to the host is involved in either nutrient acquisition or xenobiotic processing[3].

Gut Microbiota in Health: Ayurveda perspective- In Ayurvedic science, each system has its connections ultimately with gut function.

- **Digestive system**- Ayurveda has its own unique way of stating the metabolism of diet and drugs in the form of vipaka. This metabolic energy is termed *'Agni'* in Ayurveda. This can be compared to various functions that gut microbiota performs in the metabolism of carbohydrates, proteins, fats, and other nutrients in the body[4]. ***Mandangi* and microbes -** In *Mandangi* (low digestive fire), digestive enzymes are not adequate to make correct compounds. Microbes don't work properly over undigested food and form a toxic substance called "*Aam*" (body toxins) which is the root cause for most of diseases. ***Tikshagni* and microbes -** High, intense digestive fire makes the food completely burnt. Everything is converted into ash resulting in poor nutrition. ***Vishamagni* and microbes -** Undigested, digested, and partially digested food makes a toxic compound and forms a pathological condition called *Vishabdhajirn* (a type of Iô!ndigestion) which vitiates the *apan vayu* and *samana vayu*. Gut microbes don't make correct interactions with this mixture of undigested, digested, and partially digested food resulting in *Vikriti* of the digestive tract.
- **Respiratory system-** Each system in Ayurveda has been explained with the term *'strotasa'*, i.e., channels. In the case of the respiratory system, *Pranavaha srotas* (respiratory channel) have been mentioned. Also, Charak has mentioned the role of *'mahasrotasa'* (Gastrointestinal tract) which is the gastrointestinal system as the main seat of *prana* related to the respiratory system [4,5].
- **Cardiovascular system**- The heart in Ayurveda is considered under *rasa vaha* (related to the heart) and *pranavaha srotas* (related to respiratory). It is also considered to be the seat of psyche and *oja* (vitality), and any derangements in *rasa dhatu* lead to cardiovascular disease. In physiological aspects, it is clearly stated that for healthy functioning of the heart, an individual must consciously consume a diet favourable for heart and *oja* function [4,6].
- **Nervous system**- The functions of the nervous system resemble those of *Vata* (biophysical energy associated with bodily movements up to cellular level) in Ayurveda. Among five types of *vata*, *samana vata* is the enteric nervous system (ENS) which ultimately governs the entire gastrointestinal tract. In a real sense, it is the sensory stimulus of ENS (*samana vata*) that is sent to the central nervous system and resulting in vagal stimulation and gastrin feedback mechanism (*prana vata*) leading to the muscular movements, secretion of gastric juices (*vyana vata*) for digestion, absorption and discrimination [4,7].
- **Musculoskeletal system** - In the case of muscular physiology, diet plays a major role. Malnutrition results in degenerative disorders, whereas over nutrition results in the production of *'ama'* contributing to rheumatic disorders [4,8].
- **Reproductive system -** In the description of healthy spermatogenesis and oogenesis, the role of *Shadarasatmak ahara* (diet comprising six *rasas*) has been given prime importance. Thus, proper *vipaka* can result in the formation of respective healthy tissue. To have a normal and healthy conception, *hita anna sevana* (wholesome diet) has been specified in *Charak Samhita*[4].

Gut-brain axis: Ayurveda perspective

Acharya Dalhan in his commentary stated that the '*purishdharakala'* is the same as *asthidharakala*, while the *pittadhara* is similar to the *majjadharakala*. Considering the modern perspective, few efforts have been taken to establish this correlation in Ayurveda Perspective considering the majja (nervous tissues) to be present in the *Asthi* (bone marrow). However, in this scene, *majjadharakala* is thought to be associated with the nervous system and the relation between *pittadhara* and *majjadhara* can be established through modern anatomy and physiology. The *pittadharakala* is associated with the function of *pachan* (digestion) and involves the part of the GI tract. Acharya Dalhan in Kalpasthan has mentioned *pittadhara* as *majjadharakala*. No explicit explanation is found in this regard in the samhitas. However, a search into modern medicine was helpful in the interpretation of "*Pittdharasaevamajjadharaiti*". Considering the skull as the casing of the brain and the vertebrae as the casing of the spinal cord, *majja* can be associated with the entire nervous system. In the context of the above, the *majjadharakala* is associated with the nervous system[9,10]. The bidirectional pathway is based on the fact that the immune and neuroendocrine systems share ligands such as neuropeptides, hormones, cytokines, and the respective receptors. Various neuropeptides are released at the peripheral endings of sensory and efferent nerves in response to various invasive and inflammatory stimuli. Neuropeptides, such as opioids released during inflammation, possess anti-inflammatory and antinociceptive properties, which render them, potential candidates, to treat the unwanted immune responses that occur in inflammatory and autoimmune disorders, by tuning immune homeostasis in a cytokine-like manner. The above description regarding the brain-gut connection is helpful in establishing the fact stated by Dalhan about the relationship between *Pittadhara* and *majjadhara kala.*

Gut microbiota in Disease- As the intestinal microbiota is a key purveyor of mucosal homeostasis, it is consequentially implicated in the progression of these disorders.

- **Microbial Intruders of the GIT**- The invariable outcome of the infection is a disturbance in the host's gut microbial community, which has the capacity to predispose the host to further unpleasant post-infectious sequelae. Enteric pathogens utilize their arsenal of virulence factors to evoke a host response that destabilizes the indigenous microbiota and adversely affects both its protective and immunomodulatory functions [11].
- **Diseases of the GIT**- IBS including ulcerative colitis and crohn's disease have long been suspected to involve an aberrant host response to its gut microbiota. The interplay between the host microbiota and host genetics results in progressive inflammatory damage to the host's intestinal mucosa manifested through characteristic histopathological findings and associated symptomatology [11,12].
- **GIT malignancies**- The best-known and most-studied example of a microbiota-induced GIT malignancy is Helicobacter pylori-mediated gastric carcinoma. Gut microbiota composition is altered in colon carcinoma patients. Carcinoma-associated microbiota was characterized by an increase in the diversity of Clostridium spp., as well as enriched for Bacteroides and Bifidobacterium spp. Colorectal cancer (CRC) is the third leading cause of cancer-related deaths in the United States in women and second in men [13].
- **Disorders of the GIT accessory organs- a] cholelithiasis-** An involvement of the gut microbiota in the formation of gallstones has recently been demonstrated [14]. **b] Liver disease and minimal hepatic encephalopathy**- Fecal flora analysis of cirrhosis patients revealed reduced levels of beneficial Bifidobacteria [14].
- **Complex Multifactorial Disorders and Diseases of Remote Organ Systems- Obesity-** some evidence has shown the significant role of microbiota in the development of obesity [15]. **Allergy**- "Immature" microbiota delays proper maturation of the immune system, disrupting the normal sequence of events that promote the development of immunological tolerance, increasing the incidence of allergic hypersensitivity[16]. **Type 1 diabetes**- There is an important link between the gut microbiota and the development of autoimmunity, whether it is through dietary or immunomodulatory means. Type 1 diabetes (T1D) is an autoimmune disease. T1D is also linked to changes in the gastrointestinal microbiota[16,17]. **Familial Mediterranean fever and autism**- Familial Mediterranean fever (FMF) is the first genetic disease to be linked to changes in the normal gut microbiota, providing evidence that host genotype plays a role in dictating the establishment and composition of the intestinal flora. The link

between the intestinal microbiota and autism is supported by some research study observations[17].

- **Bacterial Translocation and disease-** In some circumstances, members of the gut microbiota migrate beyond their tightly regulated borders, and this disruption can cause systemic complications, promoting an entirely new repertoire of diseases targeting remote organ systems[18].
- **Major depressive disorders (MDD)-** studies prompted to hypothesize on the role of the microbiota in the regulation of Major depressive disorders, mood, and behavior and their contribution to the pathophysiology of mood disorders [19].
- **Lung Disorders-** Increasing studies indicated that alterations in the gut microbial species and metabolites have been linked to changes in immune responses and inflammation as well as disease development in the lungs. By recent increasing studies, it has been demonstrated that the gut microbiota has a critical role in mediating immune responses in distant sites, including the lung. Their metabolites such as SCFAs can reach other organs via the bloodstream to exert immune regulation and anti-inflammatory effects [21].

Vikriti vigyan pertaining to Gut Microbiota: Ayurveda perspective-

- **Neuropsychiatry-related pathologies:** Most of the manas pathological condition linked with gut microbiota is mentioned in Ayurveda contemporary literature. "*Kaphaja unmada"* (mental disease) can be correlated with the depression that was considered to result from "external factors such as tension, bereavement, loss, or a wrong diet" and is similar conceptually to the DSM-V's diagnosis of major depression'. A *vata*-induced depression, also known as *vishada*, is considered to be mild in comparison to kaphaja unmada and is usually associated with psychological rumination and worries [21]. A disturbance of *kapha* is correlated with *'manda agni'*/low *agni*, also known as hypo-metabolism, which can induce lethargy, excessive sleep, attachment, and possessiveness. When *vata dosha* is aggravated, one's *agni* becomes irregular and results in symptoms like anxiety, insecurity, cracking joints, dry skin, and insomnia. Similarly, exposure to sensory perception which increases "Tama guna" (inertia) in the mind can affect the body through this top-down mechanism. The findings suggest that the gut plays an important role in the etiology of ASD (autism spectrum disorders). A defective digestive and metabolic function are postulated as the root cause of Unmada, leading to systemic accumulation of metabolic wastes (Dhatugata ama). The metabolic wastes act as systemic toxins and impair the functional integrity of the brain. The Ayurvedic association between psychology and the gut can also be paralleled with the enteric nervous system [4,22].
- **In Metabolic Diseases:** In Ayurveda, *Madhumeha* is often regarded to share pathogenesis and clinical implication with diabetes. The pathogenesis of clearly indicates its close correlation with *Mutravaha samsthana (*urinary tract*)*, i.e., the urinary system. The genesis of urine in Ayurveda consists of its commencement in *pakvashaya* (part of the colon), which is a unique feature after the assimilation of food occurs in the alimentary canal. Ayurveda treatment regimens in diabetes strongly emphasize the establishment of a homeostatic environment primely in the gut by emesis and purgation therapies. Also, prescriptions on dietary alterations along with exercise further highlight the importance given to the gastrointestinal Tract. [23,24]
- **Diseases of Intestinal Tract:** Inflammatory bowel Diseases can be correlated to *'pravahika'* in Ayurveda. The management of *pravahika* consists of a series of medicated enemas again targeting the colon and some wholesome recipes suitable for gut health like medicated porridges and soups.[25]
- **In *Hridroga* (cardiovascular diseases):** Excessive eating, faulty timings of diet, incompatible food ingestion, faulty dietary habits as well as suppression of natural urges lead to the formation of ama. This in turn deranges the metabolism in the gut and hence hampers healthy functioning of the successive *rasa dhatu* which causes cardiovascular disorders. [25]

Concept of probiotics: Intestinal functioning is an important concept in Ayurveda and the influences of intestinal function on many disorders of the nervous system are recognized. Remedies promoted by Ayurveda include those designed to regulate intestinal function, including what we now call probiotics (provision of desirable bacteria for intestinal colonization, such as fermented products, curds, and yoghurt) and prebiotics (provision of food for desirable bacteria, such as indigestible fiber in resistant starch and complex polysaccharides). Probiotics have become widely recommended for several indications and fermented products containing bacteria are now believed to be health-promoting. It has been reported that consumption of dietary fiber enhances the production of short-chain

fatty acids (SCFAs) butyrate, propionate, and acetate by intestinal bacteria. [26]

Future perspectives-

Gut microbiota now appears to influence the host at nearly every level and in every organ system, highlighting our interdependence and coevolution. Its adaptation to our changing lifestyles (such as diet- and ethnicity-associated differences in gut microbiota composition) is astounding, highlighting that the consequences of our behaviors affect not only the environment without, but also that within us. Determining the details of the gut microbiome's involvement in our development, and function in both health and disease holds the promise of enhancing many aspects of our daily lives, from optimizing the composition of infant formulas to offering new tools in our fight against diseases related to gut microbiota.

Ayurveda resides upon the doctrine of a holistic approach. Study designs that explore the Ayurvedic *prakriti, vikriti,* and treatment modalities regarding gut Microbiota will help to offer excellent options for the healthy living of human beings.

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