Kottakkal Journal of Ayurvedic Medicine and Research
Volume 1, Issue 3 (July-September) 2025 |Page No: 15-19 | ISSN:3107-4057

ROLE OF GUT MICROBES IN GUT BRAIN AXIS AND ITS IMPLICATIONS IN *AYURVEDA* - A PILOT STUDY

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Abstract

Introduction: The gut-brain axis (GBA) refers to the communication between the central and the enteric nervous system in the wall of the GIT. This represents the links between emotional and cognitive centers of the brain with digestive functions. Studies have shown the significant role of gut microbiota in determining and modifying these interactions. Ayurveda and its approach to diagnosis and treatment is influenced by the status of digestive functions in the gut which harbours the gut microbes. **Materials and Methods:** Online databases including PubMed and Google scholar were searched for articles with keywords - gut brain axis and gut microbiome. A total of 19 articles were listed and 8 were selected from them based on their clarity of methodology, relevance and feasibility. A framework was developed after reviewing and organizing 8 articles, emphasizing the significance of *Rukshana Chikitsa* in Ayurveda for maintaining the regular functioning of the gut microbiome. These findings were validated using the tool which assesses *rukshata-snigdhata* in *koshta* among 10 participants undergoing *takrapana* and another group of 10 participants undergoing antibiotic therapy. **Results and Discussion**:73% of participants undergoing *takrapana* shows healthy *koshta*, whereas only 27% of participants undergoing antibiotic therapy show healthy koshta. Remaining participants showed increased *rukshata in koshta*. *Koshta* is an important part of clinical examination of patient in *Ayurveda*. The classification of *koshta* into *mrudu, madyama* and *krura koshta* represents a difference in the gut microbial environment. **Conclusion:** This article reviews the role of Ayurvedic principles like *Agni, koshta* and *panchakarma chikitsa* in the communication between the gut-microbiota and the brain through neural, endocrine and immune links as well as their influences on health and disease.

Keywords: Gut microbes, Gut brain axis, Ayurveda

Introduction

The human gastrointestinal tract (GIT) is an extensive interface (250-400m^2) connecting the host, environmental factors and antigens within the human body. This complex and dynamic population of microorganisms, known as gut microbiota, resides in the human gastrointestinal (GI) tract, exerting a significant impact on the host during both homeostasis and disease[1]. The gut-brain axis (GBA) indicates a two-way communication between the central and enteric nervous systems. This establishes a link between the areas of the brain related to cognition and emotion and the gastro intestinal functions[2] occurring in the periphery. In recent

times, advancements have classified the individual microbiota compositions into distinct 'community types.' A multi-dimensional analysis involving 33 samples from diverse nationalities unveiled the existence of three enterotypes distinguished by variations in the abundance of three genera: Bacteroides (enterotype 1), Prevotella (enterotype 2) and Ruminococcus (enterotype 3)[3]. The Bacteroides enterotype is linked to high-fat or high-protein diets, whereas the Prevotella enterotype is associated with high-carbohydrate diets. Recent advancements in research highlight the pivotal role of gut microbiota in influencing these two way interactions[4]. But such observation is quite lacking in the field of *Ayurveda*. This article provides a concise overview of *Ayurvedic* approaches in diagnosis, prognosis and treatment considering factors such as *Agni, koshta*, and *panchakarma chikitsa*, demonstrating bidirectional signaling between gut microbiota and the brain. This communication occurs through neural, endocrine and immune links which can have long standing effects on both human health and disease.

Rukshana therapy in *Ayurveda* produces interactions between the gut and the nervous system. It produces changes in brain chemistry and also influences neuro endocrine mechanisms related to stress, anxiety and memory. Notably, many of these effects seem to be specific to particular strains, suggesting a potential role for certain probiotic strains like *Dadhi* (curd) and *Takram* (buttermilk), as well as prebiotics like *lasunam* (garlic) and *Palandu* (onion) as a novel adjuvant strategy for neurological disorders.

Materials and Methods

To retrieve articles, an exploration was undertaken on online databases such as PubMed and Google Scholar, utilizing keywords like "gut-brain axis" and "gut microbiome." A compilation of 19 articles emerged, from which 8 were selected through screening for their thoroughness in methodology, relevance, and feasibility. These chosen articles were subsequently reviewed and structured into a framework emphasizing how *Rukshana chikitsa* sustains gut microbes. The articles strongly indicated that microbial dysbiosis signifies an excess of *rukshata* (*ati rukshata*) in the gastrointestinal tract (*koshta*).

An assessment tool was devised to evaluate *rukshata* and *snigdhata* in the gastrointestinal tract (*koshta*). In that tool (Evaluating Instrument), scores ranging from -1 to 1 were deemed ideal. Scores falling within the range of -2 to -8 were categorized as *alpa rukshata in koshta*, -9 to -15 as *madyama rukshata*, and -16 to -22 as *ati rukshata*. Upto -15 is seemed to be within physiological limit.

To substantiate the observation, ten participants undergoing *Takrapana* with *vaiswanara churna* for 7 days and ten participants undergoing a seven-day antibiotic therapy were chosen. The tool's effectiveness was confirmed in these participants and the outcomes were subsequently analysed.

Result

Among the 10 participants who underwent *rukshana kriya* with *takrapana*, an assessment using the tool revealed that 3 participants exhibited *atirukshata* in *koshta*, as indicated by a response scale exceeding -16. Conversely, 7 participants displayed *alpa* and *madyama rukshata*, which are considered to fall within the physiological limit. Similarly, out of 10 participants who underwent antibiotic medication, 8 participants showed *atirukshata in koshta.* Remaining 2 participants had *alpa* and *madyama rukshata* in *koshta*.

Table 1: Number of participants receiving *takrapana* and antibiotic medications whose *koshta* showed *atirushata* and normal within physiological limit

No. of Participants	Takrapana	Antibiotic
Atirukshata in *koshta*	3	8
Normal *koshta* (within physiological limit)	7	2

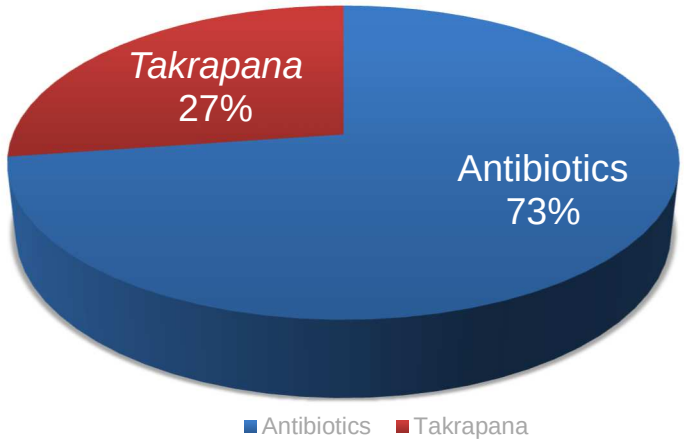

Figure 1: *Atirukshata in koshta* in participants ongoing *takrapana* and antibiotic medications

Discussion

Human beings receive various advantageous properties from the gut microbiota. The essential functions of these micro-organisms include supporting the integrity of the mucosal barrier, supplying nutrients like vitamins (Vitamin K, Riboflavin, Biotin, Nicotinic acid, Panthothenic acid, Pyridoxine and Thiamine) and offering protection against pathogens[5]. Furthermore, the interaction between commensurable microbiota and the mucosal immune system plays a vital role in ensuring proper immune function. Bacteria in the colon can also metabolize primary bile acids into secondary bile acids when not reabsorbed[6]. All these elements collectively improve the health of the host.

In the post-meal phase, enteroendocrine L cells release glucagon-like peptide-1 (GLP-1) and peptide YY (PYY). These two peptides serve as strong anorexigenic hormones and are crucial in regulating appetite. The receptors for these peptides are present at the terminal ends of the enteric neurons and vagal afferents within the gut, as well as in the central nervous system, encompassing the brain stem and hypothalamus. Typically, individuals with obesity have reduced serum levels of both GLP-1 and PYY[7]. Successfully altering the fermentation capacity of the gut microbiota has been achieved through prolonged dietary supplementation of prebiotics like *lasunam* (garlic*)* and *palandu* (onion) or probiotics like *dadhi* (curd) and *takram* (buttermilk), resulting in decreased food intake and body weight. Here, *Takrapanam* (Drinking of buttermilk) maintaining the fermentation capacity of gut microbiome, which again plays a vital role in regulating the appetite.

Enterochromaffin cells (ECs) are responsible for synthesizing the majority of 5-HT in the body from dietary tryptophan, which is obtained from *pathyahara* followed during *Takrapanam*. This neurotransmitter, 5-HT, engages a wide range of receptors on both intrinsic and extrinsic afferent nerve fibres within the gastrointestinal

(GI) tract. Its involvement extends to various GI functions such as regulating intestinal peristalsis, electrolyte secretion, pain perception and inflammatory responses[8].

Within various therapeutic categories, antibiotics emerge as the most direct and efficient means of influencing the gut microbiota. The use of antibiotics is significantly linked to alterations in the composition of the microbiota. Selective serotonin reuptake inhibitors (SSRIs), which include sertraline, paroxetine, and fluoxetine among antidepressants, exhibit antimicrobial properties against gram-positive bacteria like Staphylococcus and Enterococcus[9]. A recent study revealed that chronic administration of fluoxetine led to a reduction in caecal levels of Prevotella and Succinivibrio, as well as a decrease in Lactobacillus johnsonii and Bacteroidales S24–7. These belong to phyla associated with the regulation of body mass. Another class of antidepressants, tricyclic antidepressants (TCAs), have demonstrated the ability to inhibit the growth of gut pathogens such as E. coli, Yersinia enterocolitica, and the parasite Giardia lamblia[10]. Here use of antibiotics depleted the essential microbiome resulting in severe dyspeptic symptoms which is evident from *atiruksha lakshana* in *koshta* (GIT*)*. The gut microbiota obtains carbohydrates from intestinal mucus as well. The GI tract is filled with mucus, which is thickest in the colon and plays a critical role in mediating the host-microbiota connection there. Long-term microbial colonization is necessary for the host's intestinal mucus layers to return to normal. The two layers of colonic mucus are a loose outer layer that germs may penetrate and an interior layer that is tight and impenetrable[11]. *Takram* (buttermilk) helps to maintain the level of primary bile acids such as taurocholate and can help spores germinate by giving gut bacteria homing cues. Additionally, it could make microbiota recovery easier following antibiotic- or toxin-induced dysbiosis. The host immune system can also influence the microbiome. Numerous environmental variables such as geographic location, surgery, smoking, depression, and living conditions (urban or rural), have been linked to the development of the microbiota. The physiology and gene expression of the human gut microbiome in action may also be influenced by xenobiotics[12].

Ayurvedic treatment approaches consistently rely on preserving the microbiome to maintain *jataragni*. This *jataragni* is related to important aspects of human Gut Brain axis. Microbial depletion can lead to dyspeptic symptoms, corresponding to *atirukshata* in *koshta*, indicating a decline in the functioning of *jataragni* (*mandagni*). In the presence of *atirukshata* in *koshta* (*mandagni*), the hypothalamus releases corticotropin-releasing factor (CRF), activating the Gut-Brain axis in response to heightened systemic pro-inflammatory cytokines and environmental stress caused by microbiome depletion. This activation prompts the pituitary gland to release adrenocorticotropic hormone (ACTH), stimulating the adrenal glands to produce cortisol, a key stress hormone affecting brain and organ functions. Brain involvement simultaneously impacts the functions of various intestinal effector cells, including immune cells, epithelial cells, enteric neurons, smooth muscle cells, interstitial cells of Cajal, and enterochromaffin cells, influenced through a combination of neurological and hormonal communication pathways.

Conclusion

The gut microbiota plays a crucial role in interactions between the gut and the nervous system. This interaction involves the regulation of neurotransmitters in the brain and influence on neuro-endocrine systems associated with stress, anxiety and memory function. The specific effects often appear to be strain-dependent, hinting at the potential use of particular probiotic strains as an adjuvant strategy for neurological disorders. In this context, the *Ayurvedic* treatment approach known as *Takrapana* holds significant importance in sustaining a healthy gut microbiome.

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