

The Physiological Understanding About Pachkagni (Digestive Fire) And Gut Microbiota In Context With Gut – Liver Axis And Gastrointestinal Tract (GIT) – An Integrative Review

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Abstract

Introduction: According to Ayurveda, understanding Pachkagni (digestive fire), Gut microbiota and Gut-Liver axis at the level of Gastrointestinal Tract (GIT), is the key to understand the physiology and pathology of body. In Ayurveda, Pachkagni (digestive fire) plays important role in dietary recommendations, lifestyle modalities and the treatment Protocol for various disease. According to modern medicine, Gastrointestinal (GI) tract comprising of approximately 100 trillion of bio-organisms. In special context with Gut-liver axis, the modern science details about the Gut microbiota, an ecosystem of bio-organisms, required for digestion, assimilation and overall immunity.

Methodology: A comprehensives literature-based approach was adopted. Literatures were reviewed from ancient Ayurvedic and modern science textbooks with published research databases like Scopus, Web of science, PubMed, using keywords such as “Pachkagni,” “digestive fire,” “Srotasa,” “microbiota,” “gut-Liver axis,” “dysbiosis,” and “GIT.” The present review explores the physiological understanding using contemporary literature discussing Pachkagni (digestive fire) and Gut microbiota with the Gut-liver axis and Gastrointestinal Tract (GIT).

Results: The research analysis presents significant similarities and correlations between the functioning of Pachkagni and the Gut microbiota. Both supports each other in digestion, Gut-Liver communication, immune modulation and inflammation control. The gut-liver axis is an established, bidirectional link connecting the Gut or GIT with liver (functional site of Pachkagni), which is important for the maintenance of body metabolism.

Discussion: Pachkagni and the Gut microbiota show a common significance in the homeostasis of metabolism. The integration of Gut-liver axis in GIT, targets a challenging correlation of Ayurvedic and modern medicine. In Ayurveda, the activities of Pachkagni (digestive fire) are dependent on the balanced functioning of Liver, since the disturbances of Pachkagni (digestive fire) results in accumulation of Ama (toxic metabolite), which is conceptually mirrored with the Gut dysbiosis in modern medicine. By integrating the Ayurvedic metabolic wisdom with contemporary microbiome concepts, the present research has targeted a personalized and holistic approaches in context with healthy GIT.

Keywords: Pachkagni, Gut, Microbiota, GIT, Dysbiosis, Gut-Liver axis, Digestive fire.

Introduction:

In Ayurveda, Pachkagni (digestive fire) is considered as the foundational principle of the well-being as the root (mool) of health and longevity ^[1]. The major focus of Pachkagni (digestive fire) is to perform digestion and metabolism of ingested food products and nourishment of body at cellular to systemic level. Pachkagni (digestive fire) manages the normal physiological activities by transforming the food into power, so referred as Bio-transformer ^[2]. On the other hand, any disturbance or vitiation of Agni from its Sama position, hampers the metabolism, resulting in disturbed health and the origin of diseases. The Normal Pachkagni (Sama) will facilitates digestion and physiological health. While, Abnormal Pachkagni, digestive fire (Manda or Vishama) will lead to diminished Gut microbiota ecosystem, diminished value of absorbable essence, disturbed gut-Liver axis signaling. The correlation among Pachkagni (digestive fire) and Gut microbiota, shows a special significance in terms of contemporary knowledge according to various digestive stages of Pachkagni (digestive fire), in management of the various aspects of Gut microbiota and GIT. The system of modern medicine confirms the importance of Gut microbiota in facilitating digestion in GIT, with dysbiosis. The disturbance of Pachkagni (digestive fire) results in the accumulation of Ama (toxic metabolite), which is identical to Gut dysbiosis and systemic inflammation according to modern medicine ^[4].

The Gut microbiota, constitutes of trillions of different types of intrinsic bio-organisms like bacteria, fungi, archaea, and protozoa, which remains in a synergistic relationship with the human intestine ^[5]. Usually, the ecosystem of Gut microbiota remains uniform in GIT, but may vary due to variety of components like food habit, lifestyle, body mass index (BMI), exercise and cultural adaptations ^[6]. According to modern medicine, the Gut

microbiota has been identified as the principal key of digestion, metabolism, immunity, and neuropsychological health. The modern medicine research has unfolded that the alternation in the ecosystem of gut microbiota, results in enhanced physiological activities of GIT. The modern medicine interventions used in maintenance of GIT such as probiotics, prebiotics and anti-inflammatory food are correlated with Ayurvedic interventions like Deepana (stimulating Agni), Pachana (digesting Ama) and Rasayana (rejuvenation therapies).

The liver is considered as an important immunological organ, which is regularly exposed to Gut-originated nutrients, metabolites and endotoxins [5]. The Gut-liver axis defined as a two-way interaction key among the Gut microbiota and the liver for demonstrating an important role in improving immunity, detoxification and regulating metabolism [7]. The disturbance in the Gut microbiota, is defined as dysbiosis, which has ability to disturb the Gut integrity and passing of undigested harmful particles into the liver to produce inflammation and oxidative stress in the parenchyma of Liver, exhibiting key attributes in the development of various liver disorders. The research Findings demonstrate similarities among the physiological and pathological functioning of Pachkagni (digestive fire), Gut microbiota and the gut-liver axis as per modern medicine. Both system of medicine impact over the digestive and metabolic integrity in systemic health and disease manifestation.

Objective: To explore the conceptual and functional correlation between Pachkagni (digestive fire) and Gut Microbiota in special context with Gut-Liver axis in Gastrointestinal Tract (GIT), integrating the ancient Ayurvedic concepts and modern microbiological references.

Methodology

A comparative analytical review was performed using ancient Ayurvedic texts books, Ayurvedic reference books using authentic English translations and commentaries, along with the modern medicine books focusing on publications related to Gut microbiota, metabolism, inflammation, Gut-liver axis and Gastrointestinal Tract and also, a well-planned search was conducted among major research databases like Scopus, Web of Science, PubMed, AYUSH Research Portal and Google Scholar, using keywords "Pachkagni," "digestive fire," "Srotasa," "microbiota," "Gut-Liver axis," "dysbiosis," and "GIT". The present review explores the physiological understanding using contemporary literature discussing Agni and Gut Microbiota with the Gut-liver axis and Gastrointestinal Tract (GIT).

In contemporary scientific literatures from online research journals, areas were identified from to understand Gut – microbial ecosystem, Gut–microbe interactions, and their role in health and disease. More attention must be exerted for elaborating the activities of digestion, metabolism, Gut-liver interactions, GIT and their systemic effect instead of only microbiota ecosystem. Hypothetical integrations were employed via detailed analytical procedure which can compare the subjects like digestion, metabolism, metabolic efficiency, Ama (toxin metabolites), Dysbiosis, immunity and Gut-liver interaction to interpret and establish the integrative research work.

In this present review PRISMA guidelines were not followed, since it is purely literary and theoretical using references from text books, fully devoid of meta-analysis or systemic review without presence of flow diagram. During this review any sort of experimental studies, clinical studies or laboratory-based methods were adopted as part of this study. This review article does not represent any scooping, primary data collection, patient outcomes or statistical analyses.

The original observational reviews were obtained to collect the literary and narrative interpretations which alone cannot be properly achieved through quantitative meta-analysis.

Literature Review

Pachkagni (digestive fire)

According to Charaka, Agni is considered as an important Karana Dravya (causative factor) of the human body and also identified as basic power behind all transformations in body. According to Marich, Agni residing in Pitta dosha, performs all physiological activities, resulting the condition of healthy, when balanced and resulting in condition of unhealthy, when impaired [8]. According to Sushruta, Pitta dosha himself is Agni and no other form of Agni found in human body, since the functional properties of pitta dosha is similar to the functional properties of Agni in all aspect, Like the Tikshna (sharp) and Ushna (hot) properties of Agni are identical to Pitta dosha, performing the activities like Dahana (burning) and Pachana (digestion). According to the classification of Agni, there are is thirteen types of Agni, with Pachkagni, the digestive fire, functionally sited in the Liver and Grahani (small intestine) and considered as most important in context with Gut microbiota and Gastrointestinal Tract

(GIT). This Pachkagni (digestive fire) greatly impact the other metabolic forms of Agni, like five types of Bhutagni and seven types of Dhatvagni, which are transforming the five elements (Panchamahabhuta) and body tissues (Dhatus) ^[9]. Based on its functional aspect of digestion or the metabolic aspect of its digestive fire, Agni is generally considered and defined as Pachkagni (digestive fire), since it that type of Agni which function in collaboration with Pachak pitta and involved in the process of digestion and metabolism.

The Pachkagni (digestive fire) is responsible for digestion, metabolism, and transformation of the body at cellular level to systemic level, since it helps in the absorption of nutrients and the maintaining homeostasis of all metabolic activities of body. In the view of digestion or metabolism, the power of Pachkagni (digestive fire) is classified in four conditions i.e., Samagni (balanced), Tikshnagni (hyperactive, linked to Pitta dosha), Mandagni (diminished, associated with Kapha dosha), and Vishmagagni (irregular, related to Vata dosha). The Maintenance of balanced condition of Agni, is very crucial for the sustenance of life, since it facilitates the breakdown and assimilation of food, for the maintenance at cellular level and immunity. Disturbance in the condition of Pachkagni (digestive fire), is treated the main reason for majority of diseases like impaired digestion and metabolism which results in formation of Ama (Toxic metabolite), which obstructs the minute channels of body (Srotas) and affects the physiological functions of body. The functional properties of Ama (Toxic metabolite) are identical to Dysbiosis, which results from disturbed Gut microbiota like Pachakagni (digestive fire).

Classification of various Pachkagni stages and Gut Microbiota

1. Tikshnagni (Intense state of digestive fire) – It is identified as rapid onset of digestion, facilitating abnormal assimilation, characterized by the dominance of Pitta dosha and resulting in conditions like inflammation and hyperacidity. The microbiota ecosystem in Tikshnagni manifests in reduced microbial diversity due to inflammation or hyperacidity due to intense metabolic activity. This results in increased pro-inflammatory microbial species like Proteobacteria, followed by decreased populations of Short-chain fatty acid (SCFA)-producing bacteria like Faecalibacterium prausnitzii and Roseburia.

2. Mandagni (Low or weak state of digestive fire) - It is identified as weak or low onset of digestion, characterized by the dominance of Kapha dosha, facilitating the generation of Ama (toxins) and resulting in conditions like heaviness and lethargy. The microbiota ecosystem in mandagni manifests in reduced microbial diversity, suggesting dysbiosis. This results in increased quantity of pathogens and fermentative bacteria, resulting excessive gas and toxin production. This microbiota species is needed for carbohydrate and protein metabolism and decreased populations of short-chain fatty acid (SCFA), impacting the gut-brain and gut-immune transmissions.

3. Vishmagagni (Irregular state of digestive fire) – It is identified as irregular onset of digestion, characterized by the dominance of Vata dosha, facilitating the conditions like hyperactivity and sluggishness, and resulting in conditions like bloating, gas and irregular bowel movements. The microbiota ecosystem in Vishmagagni manifests in fluctuations of microbial diversity, suggesting unstable gut conditions. This results in dominance of Stress-sensitive microbial species, indicating disturbance in the gut-brain axis. Additionally, the prevalence of methane-producing bacteria, especially Methanobrevibacter smithii, indicated to irregular intestinal motility. The episodic disturbances of Short-chain fatty acid (SCFA), suggesting irregular fermentation within the gut.

4. Samagni (Balanced state of digestive fire) – It is identified as the balanced stage of state of digestion, characterized by the balanced equilibrium of all three dosha, resulting adequate nutrient absorption. The microbiota ecosystem in Samagni, manifests in high microbial diversity, resulting healthy gut microbiota like Bacteroidetes, Firmicutes, and short-chain fatty acid (SCFA) producers like Faecalibacterium, Akkermansia and Bifidobacterium. This balanced microbial ecosystem supports anti-inflammatory and immune-modulatory functions, exhibiting healthy gut lining.

Pachkagni and Gut-Brain Axis ^[10]

The normal power of Pachkagni (digestive fire) facilitates the proper digestion, ensuring the availability of necessary nutrients for maintenance and nourishment of the body's tissues (dhatus), which contribute to the overall health and vitality of body, in terms of strength, complexion and immunity. The diminished power of Pachkagni (digestive fire) impairs the digestion and assimilation of nutrients, which results in improper health of body. The Gut-brain axis (GBA) comprises of bidirectional integration among the enteric nervous system (ENS), the central nervous system (CNS) and Gut microbiota with Gastrointestinal Tract (GIT), proliferating the important role in digestion, immunity and mental health. Similarly in Ayurveda, the bidirectional integration among Pachkagni (digestive fire), Saman Vayu and Grahani (small intestine) communicate through Manovaha Srotas (mind-body channel) in maintenance of metabolic health and general digestion, can be mirrored with the

Gut Microbiota: A Modern Perspective

According to modern medicine, Gastrointestinal (GI) tract comprising of approximately 100 trillion of bio-organisms, which counts around ten times of the somatic cells in human body. The colonies of these bio-organisms are promoting a symbiotic relationship with their host. The word "microbiota" defined as the group of bio-organisms like bacteria, archaea and some variety of unicellular eukaryotes, living in suitable environments of the stomach, mouth, and skin ^[11]. Bio-organisms in GIT, differ in colony, quantity and their function with maximum quantity found in the large intestine. The Gut microbiota contribute towards fermentation of undigested food components, particularly carbohydrates and fibrous material which forms the waste bulk for excretion. The most efficient bacterial species in human gut are Bifidobacterium, Lactobacillus, Bacteroides, Clostridium, Escherichia, Streptococcus and Ruminococcus, which contribute towards 60% of total microbiota ecosystem specified under the category of phyla Bacteroidetes or Firmicutes ^[12]. The gut microbiota is responsible for metabolizing the food components, which is difficult for normal human body enzymes to digest the ingested food material like complex polysaccharides. These are further converted into short-chain fatty acids (SCFAs) with acetate, propionate, and butyrate, which are responsible for the energy production of colonocytes, immunity regulation, and the maintenance of the intestinal barrier ^[13]. Apart from this, the gut microbiota manifests essential vitamins like vitamin K and certain B vitamins, which is important for all the metabolic activities. Along with its metabolic activities, the gut microbiota is also known for improving and modulating the immune system ^[14]. Gut microbiota proliferates immune cell maturation, initiates pro-inflammatory and anti-inflammatory responses, and protection from the pathogens via exclusion and antimicrobial production ^[15]. In total, the gut microbiota communicates with ENS and CNS through the Gut-brain axis, impacting the brain physiology and behaviour ^[16].

Gut-Liver axis

The Gut-Liver axis comprises of the mutual integration among the Gut and the liver, communicating through the bloodstream, portal vein and bile ducts. This interconnection depends on two primary area:

- a) Gut microbiota
- b) Gut barrier

Gut microbiota and Gut-Liver axis

The physiological Gut-Liver axis depends on the physiological equilibrium of bile acid and enterohepatic circulation ^[17]. In this axis, the Gut-digested essence is carried through portal vein, straight to the liver, on the other hand, the liver generates bile acids into the small intestine. The Gut microbiota have large impact over the liver via both route of bacterial metabolites and the intestinal barrier ^[18]. In routine physiological conditions, the liver and small intestine generate bioactive compounds which either communicate with each other or with the Gut microbiota. The Intestinal bio-organisms reforms a wide variety of metabolites, which can influence the permeability of intestinal barrier or can be absorbed by intestinal parenchyma. After intestinal absorption across mucosa, the metabolites transported via portal vein to the liver, where these metabolites influence the liver activities. The Gut microbiota is greatly dealing with the liver diseases via various activities like increased intestinal permeability, chronic systemic inflammation and disturbance in bacterial metabolism.

Gut barrier and Gut-Liver axis

The physiological Gut barrier is important in maintaining the intestinal integrity, which acts as structural and functional integrity, which maintain connection among the Gut and liver, maintaining the communication between Gut-Liver axis ^[19]. Its interaction is divided in three types of layers. The outermost layer is made up of mucus coming from the intestinal goblet cells and rich in mucin protein. This layer also develops an environment for microbiota maintaining direct connection among bacteria and epithelial cells. Beyond this epithelial layer, the lamina propria (LP) is present, where these immune cells create the Gut's immunity barrier ^[20]. The immune cells of these immunity barrier, show a defined role in generation of defensive action against metabolic pathogens, which enters the intestinal parenchyma. In ideal conditions, the intestinal metabolites crosses via different layers of Gut barrier, showing the mediated microbiota transfer, before entering the liver across Gut-liver axis.

Dysbiosis

Dysbiosis refers to the disturbance at the level of Gut microbiota ecosystem, characterized by decreased

microbiota activity and development of pro-inflammatory variety. This type of Dysbiosis results from unhealthy lifestyle choices like sustained alcohol consumption, excessive food consumption and diminished physical activity. All these factors put great emphasis over Gut microbiota, resulting in dysbiosis ^[21]. It is generally associated with the compromised intestinal barrier activity (often termed leaky gut), discharge of endotoxins, disruption in bile acid composition and reduced choline concentrations ^[22]. These modifications enable the gut microbiota, with its metabolites and Extracellular Vesicles (EVs), enters the intestinal barrier and penetrate inside the portal circulation, which leads towards liver diseases. In large, liver disorders are greatly impacted by Gut microbiota by influencing the bile acid circulation ^[23].

Gastrointestinal Tract (GIT) and Gut-brain axis

The Gastrointestinal Tract (GIT) is maintained by the ENS, which is further controlled by the central nervous system (CNS) and sympathetic nervous system. The GIT consists of a complete web or a neural bed of sensory neurons, motor neurons, and interneurons embedded deep inside in the wall of Gut throughout its lumen which stimulates the GIT starting from the bottom third of the oesophagus till the rectum. The neural intervention to the oesophagus, stomach, liver, gall bladder, pancreas, entire small intestine and proximal half of the colon, is supplied by the cranial parasympathetic nerve fibers. The neural intervention to the descending colon, rectum, urinary bladder, is supplied by the sacral parasympathetic fibers. The myentric and submucosal plexus, are carrying the post ganglionic neurons of gastrointestinal parasympathetic system. The activity of ENS, is greatly stimulated through these nerve fibers. The neural branches of sympathetic fibers of GIT, are initiating from the spinal cord between T7 T-11 segment. Majority of the preganglionic fibers remains out of the spinal cord before entering the sympathetic fibers chain. While, very few preganglionic nerve fibers enter with spinal cord origin without synapsing through the sympathetic fibers chain to merge with pre vertebral ganglia such as celiac ganglia and mesenteric ganglia, further merges into postganglionic nerves supply throughout the Gut. The activity of GIT is stimulated by the sympathetic nerve fibers due to direct impact of secreted norepinephrine, which inhibits either the smooth muscle fibres of GIT or the nerve fibers supply of ENS ^[24].

Result and Discussion:

The Pachkagni (digestive fire) is considered as the key to Ayurveda since, it is responsible for the efficiency of digestion, absorption, and metabolism. The Pachkagni (digestive fire) is physiologically influencing the Gut microbiota according to its various functional types. In Ayurveda, the body's functional channels (Srotas) are treated as the route for the travelling of all essential products throughout the body and disturbance to these channels, creates the disease. In conditions like Manda Agni, can result in accumulation of Ama (toxins), which further initiates the systemic inflammation and may aggravate the disease conditions ^[25]. This situation of Ama accumulation, can be mirrored with the conditions like Dysbiosis in gut microbiota, which is represented as the increased colonies of pathogenic Enterobacteriaceae and decreased colonies of beneficial Lactobacillus and Bifidobacterium species ^[26].

In conditions of Tikshna Agni, it can result in aggressive metabolism which results in dehydration and increased gut permeability, representing exposure to gastrointestinal infections ^[27]. Dysbiosis is also affecting the Annavaha Srotas (food channels), which is dealing with the food digestion and nutrient assimilation and disturbance by conditions such as anorexia, indigestion, constipation and GIT disorder like irritable bowel syndrome (IBS). Recent Studies shows that the different quantity of the Firmicutes and Bacteroidetes, with increased Methanobrevibacter species, leads towards to constipation and bloating ^[28]. In the condition of Manda Agni, the diminished process of digestion and Ama formation, results into formation of condition like Dysbiosis and also worsening GIT disorder like IBS, while in situation of Vishama Agni results in irregular digestion and microbial fluctuations. The impaired digestion and nutrient absorption in Mand Agni, also results in Pandu (anaemia) and metabolic deficiencies across GIT. Manda Agni leads to neuroinflammation and cognitive dysfunction, whereas Vishama Agni contributes to fluctuating mental states and reproductive imbalances. This earlier discussion reveals that ancient Ayurvedic scholars are following and understanding the application of Gut dysbiosis in coordination with the practical application of Pachkagni (digestive fire) in various aspects and pathological conditions.

Gut microbiota possess physiological similarity with Pachkagni (digestive fire) in digestion, absorption, assimilation and other metabolic activity in human body, it also shows a vital involvement in catabolism of food, synthesis of essential nutrients and immunity maintenance. The balanced condition of Pachkagni (digestive fire) is responsible for stable health, like balanced Gut microbiota ecosystem, is responsible for the enhanced digestion, immunity and mental stability. Gut microbiota imbalances, results in overgrowth of Desulfovibrio

variety, which enhances endotoxin production, resulting in conditions like inflammation and oxidative stress in blood and skin-related diseases ^[29]. In Gut microbiota, Dysbiosis is the disturbance in the normal ecosystem of microbiota, comprises of low production of beneficial metabolites like short-chain fatty acids (SCFAs) while increased production of harmful metabolites like lipopolysaccharides (LPS). This disturbed microbiota ecosystem will compromise the permeability of the intestinal barrier, results in enhanced permeability, known as “leaky Gut.” If the permeability of intestinal barrier is breached by microbial components such as LPS, it enters the portal circulation and reaches the liver.

According to Ayurveda, Liver is possessing functional similarities with Pachkagni (digestive fire) in terms of its physiology and location attributes. According to recent advancements, it is suggested that many factors, like unhealthy diet, dysbiosis and chronic inflammation, hampers the Gut barrier. This hindrance results in the Gut leakage of viable bacteria, their components and metabolites, resulting liver disease like dysbiosis, which attributes towards hepatic steatosis (fatty liver) and liver-related inflammatory processes. Disturbance among Gut-liver axis happens due to faulty communication among Gut and liver, which usually happens in Gut dysbiosis, increased intestinal permeability and intestinal imbalance.

The Gut-liver axis identifies as an essential physiological communication, where the liver activities detoxify and metabolize the essential nutrients obtained from the intestines through portal vein before circulating throughout human body. The activity of Pachkagni (digestive fire) and the Gut-liver axis, both have great impact over digestion and metabolism in maintaining the well-being. The digestion and assimilation of essential nutrients by Pachkagni (digestive fire) is in tune with the Gut-liver axis's activities of processing nutrients and toxins. Disturbance in Pachkagni (digestive fire), results in disturbed tissue nourishment and formation of disease like malfunction of the Gut-liver axis, results in metabolic disorders, inflammation, and toxin accumulation.

In future, the research studies must analyse this integrative approach with the help of molecular research and further clinical evaluations, showing the path for research-based contemporary approach, which intermingle ancient Ayurvedic wisdom with the depth of modern medicine. This methodology with excellent potential strengthens the integrative research and evidence-based clinical models.

Conclusion:

According to Ayurveda, Pachkagni (digestive fire) is considered as the principal modulator of digestion, metabolism, energy production, and overall systemic health; so also referred as “Bio-transformer” of the Human body and its disturbance, results in accumulation of Ama (Toxin substance) formation identical in functions to Dysbiosis process in the conditions of Disturbed Gut microbiota, which finally contribute towards development of disease. Similarly, Modern medicine, treats Gut microbiota as a principal modulator of digestion, metabolism, energy production, immunity through Gut–liver axis. The integration of Pachkagni (digestive fire) and Gut microbiota offers a contemporary approach in knowing the digestive and metabolic approach. In Ayurveda, the food and lifestyle modalities, narrates clear positive direction for the importance of Gut microbiota and metabolic balance with reduced risk of disease. This integration brings hope for a resulting evidence-based physiological understanding about pachkagni (digestive fire) and gut microbiota in special context with gut – liver axis and Gastrointestinal Tract (GIT) with this present research model of digestive wellness. Irrespective of hypothetical similarities, direct scientific evidence among this Ayurveda and biomedical approach, needs to be explored further. These types of integrative frameworks, which guide the Pachkagni (digestive fire) based Ayurvedic learning with gut-liver axis and Gastrointestinal physiology, may further showcase a comprehensive idea for the prevention and management of gastrointestinal and Liver disorders.

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References

1. Agnivesha, Charaka, Dridhabala. Charaka Samhita, Chikitsasthana, 15/4. In: Acharya VJ, editor. Reprint edition. Varanasi: Krishnadas Academy, 2013, p. 453.
2. Vaidya Yadavji Trikamji Acharya, Charaka Samhita by Agnivesha with Ayurveda Dipika Commentary of Chakrapanidatta, Chikitsa Sthana; Chapter 15, Verse 3. Varanasi: Chaukambha Krishnadas Academy, 2023; P.512
3. Agnivesha, Charaka, Dridhabala. Charaka Samhita, Chikitsasthana, 15/5. In: Acharya VJ, editor. Reprint edition. Varanasi: Krishnadas Academy, 2013, p. 453.
4. Afnan N, Shivaprasad SE, Patil AS. Understanding relationship between concept of Agni, Ama and Gut Brain Axis – Contemporary Review. J Ayurveda Integr Med Sci. 2025;10(1):223–226.
5. Wang R, Tang R, Li B, Ma X, Schnabl B, Tilg H. Gut microbiome, liver immunology, and liver diseases. Cell Mol Immunol.

2021; 18:4–17.

6. Park KJ, Gao Y. Gut–brain axis and neurodegeneration: mechanisms and therapeutic potentials. *Front Neurosci.* 2024;18.

7. Zhang X, Liu H, Hashimoto K, Yuan S, Zhang J. The gut–liver axis in sepsis: interaction mechanisms and therapeutic potential. *Crit Care.* 2022;26.

8. Agnivesha, Charaka, Dridhabala. *Charaka Samhita, Sutrasthana, 12/11.* In: Acharya VJ, editor. Reprint edition. Varanasi: Krishnadas Academy, 2013.

9. Agnivesha, Charaka, Dridhabala. *Charaka Samhita, Sutrasthana, 12/11.* In: Acharya VJ, editor. Reprint edition. Varanasi: Krishnadas Academy, 2013.

10. Veena M, Sivaram A, Pradeep K. The role of Agni in epilepsy–A Scoping Review. *Kerala Journal of Ayurveda.* 2024 Dec 30;3(4). DOI: <https://doi.org/10.55718/kja.324> [last accessed 01.12.2025].

11. Singh V, Rao MV. Seasonal regimen (Ritucharya) with special reference to Agni and gut microbiota. 2024 Dec;15(S1):157–163. DOI: 10.47552/ijam.v15iS1.5588 [last accessed 01.12.2025].

12. Backhed, F.; Ley, R.E.; Sonnenburg, J.L.; Peterson, D.A.; Gordon, J.I. Host-bacterial mutualism in the human intestine. *Science* 2005, 307, 1915–1920. DOI:10.1126/science.1104816 [last accessed 01.12.2025]

13. Wong JM, de Souza R, Kendall CW, Emam A, Jenkins DJ. Colonic health: fermentation and short-chain fatty acids. *J Clin Gastroenterol.* 2006 Mar;40(3):235–43. doi: 10.1097/00004836-200603000-00015. PMID: 16633129. [last accessed 01.12.2025]

14. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I, Tuohy K. Gut microbiota functions: metabolism of nutrients and other food components. *Eur J Nutr.* 2018 Feb;57(1):1–24. doi: 10.1007/s00394-017-1445-8. Epub 2017 Apr 9. PMID: 28393285; PMCID: PMC5847071. [last accessed 01.12.2025]

15. Chu J, Feng S, Guo C, Xue B, He K, Li L. Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: A review. *Biomedicine & Pharmacotherapy.* 2023 Aug 1; 164:114985. <https://doi.org/10.1016/j.biopha.2023.114985> [last accessed 01.12.2025]

16. Zhu X, Han Y, Du J, Liu R, Jin K, Yi W. Microbiota-gut-brain axis and the central nervous system. *Oncotarget.* 2017 May 10;8(32):53829–53838. doi: 10.18632/oncotarget.17754. PMID: 28881854; PMCID: PMC5581153. [last accessed 01.12.2025].

17. Blesl A, Stadlbauer V. The gut–liver axis in cholestatic liver diseases. *Nutrients.* 2021;13:1–32.

18. Zhang S, Wang Q, Tan DEL, Sikka V, Ng CH, Xian Y, et al. Gut–liver axis: potential mechanisms of action of food-derived extracellular vesicles. *J Extracell Vesicles.* 2024;13.

19. Pabst O, Hornef MW, Schaap FG, Cerovic V, Clavel T, Bruns T. Gutliver axis: barriers and functional circuits. *Nat Rev Gastroenterol Hepatol.* 2023; 20:447–61.

20. Zheng Z, Wang B. The gut–liver axis in health and disease: the role of gut microbiota-derived signals in liver injury and regeneration. *Front Immunol.* 2021 Dec 10;12.

21. Leung C, Rivera L, Furness JB, Angus PW. The role of leaky gut in nonalcoholic fatty liver disease: a review. *Int J Mol Sci.* 2021;22 (15):8161.

22. Sharma S, Tiwari N, Tanwar SS. The current findings on the gut–liver axis and the molecular basis of NAFLD/NASH associated with gut microbiome dysbiosis. *Naunyn Schmiedeberg Arch Pharmacol.* 2025 Apr 9.

23. Tilg H, Adolph TE, Trauner M. Gut–liver axis: pathophysiological concepts and clinical implications. *Cell Metab.* 2022 Nov;34(11):170018.

24. Hall. E, Guyton. C. *Gastrointestinal physiology, Textbook of medical physiology*, New Delhi (India), Elsevier; 2006:777.

25. Yadav PV. Medical Perspective on Ama as per Ayurveda and Modern Consideration: A Review. *Journal of Drug Delivery & Therapeutics.* 2020 Feb 1;10. DOI:10.22270/jddt.v10i1s.3861 [last accessed 01.12.2025]

26. Carding S, Verbeke K, Vipond DT, Corfe BM, Owen LJ. Dysbiosis of the gut microbiota in disease. *Microbial ecology in health and disease.* 2015 Dec 1;26(1):26191. <https://doi.org/10.3402/mehd.v26.26191> [last accessed 01.12.2025]

27. Mengaji R. Critical Study on Vikalp-Samprapti in Grahani Vyadhi to Bruhstrayi (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)). [last accessed 01.12.2025]

28. Pozuelo M, Panda S, Santiago A, Mendez S, Accarino A, Santos J, Guarner F, Azpiroz F, Manichanh C. Reduction of butyrate- and methane-producing microorganisms in patients with Irritable Bowel Syndrome. *Scientific reports.* 2015 Aug 4;5(1):12693. [last accessed 01.12.2025].

29. Singh SB, Carroll-Portillo A, Lin HC. Desulfovibrio in the gut: the enemy within?. *Microorganisms.* 2023 Jul 7; 11 (7) : 1 7 72. <https://doi.org/10.3390/microorganisms11071772> [last accessed 01.12.2025].