

## Understanding relationship between concept of Agni, Ama and Gut Brain Axis - Contemporary Review


Naaz A<sup>1\*</sup>, Shivaprasad SE<sup>2</sup>, AS Patil<sup>3</sup>

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- <sup>1\*</sup> Afnan Naaz, Post Graduate Scholar, Department of Roga Nidana Evum Vikriti Vigyana, Govt Ayurveda Medical College, Bangalore, Karnataka, India.
- <sup>2</sup> Shivaprasad SE, Assistant Professor, Department of Roga Nidana Evum Vikriti Vigyana, Govt Ayurveda Medical College, Bangalore, Karnataka, India.
- <sup>3</sup> AS Patil, Professor and HOD, Department of Roga Nidana Evum Vikriti Vigyana, Govt Ayurveda Medical College, Bangalore, Karnataka, India.

Hippocrates of kos, a Greek physician widely regarded as the founder of modern medicine, said that All diseases originate in the gut, "even though acharya *Charaka* had already emphasized the significance of *Agni* (the digestive fire) when he said that "the causes of all disease is *Mandagni*. Due to hypofunction of *Jatharagni* result into the formation of the *Ama*. *Ama* is the improper digestion or partially digestion of the food particle accumulation of *Mala* in the body and also considered as *Prathamdoshadusti*". Gut bacterial flora can impact the physiology of the central nervous system (CNS) and play a significant role in pathological diseases. The Gut microbiota has extensive reciprocal connection with the human brain through microbial metabolites, the vagus nerve, spinal nerve, hormonal & immunological signalling, collectively forming the microbiome gut -brain - axis. Life style factors such as eating junk food, sleep patterns, stress levels, less physical activity, and medication use also influences the gut microbiome. Chronic stress and inadequate sleep can disrupt microbial balance and releases various metabolites. Dysbiosis has been linked to various health conditions, including gastrointestinal disorders, metabolic disease like obesity & diabetes, autoimmune disorders, allergies, and mental health issues such as depression and anxiety etc. Here we discuss about structure and Functions in both entities, which are similar and dissimilar, also whether dysbiosis, microbial metabolite can be considered under *Agnidusti* and *Ama* respectively. The present article attempts to understand the relation of *Agni*, *Ama* and gut brain axis in pathogenesis of diseases.

**Keywords:** Ama, Agni and Gut-Brain-Axis

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Afnan Naaz, Post Graduate Scholar, Department of Roga Nidana Evum Vikriti Vigyana, Govt Ayurveda Medical College, Bangalore, Karnataka, India. Email: <a href="mailto:affinaaz2424@gmail.com">affinaaz2424@gmail.com</a>	Naaz A, Shivaprasad SE, AS Patil, Understanding relationship between concept of Agni, Ama and Gut Brain Axis - Contemporary Review. J Ayu Int Med Sci. 2025;10(1):223-226. Available From <a href="https://jaims.in/jaims/article/view/3961">https://jaims.in/jaims/article/view/3961</a>	

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## Introduction

Ayurveda states the importance of *Samadosha*, *Samagni*, *Samadhatu*, *Malakriya Prasanna Atma Indriya* for A healthy lifestyle.[1] *Agni* is the governing process of digestive system. *Sanskrit* word that translates as digestive fire. *Agni* is associated with digestion, metabolisms and assimilation of nutrients.[2] The site of *Agni* is *Grahani* it is so called because of power to retain the food, it is situated above the umbilical region and is supported and nourished by the strength of the *Agni*. When *Agni* disturbed it considered to promote the *Ama* formation the treatment in ayurveda revolves around the modulation and management of *Agni*. [3] *Agni* are 4 types *Samagni*, *Vishamaagni*, *Tikshna Agni*, and *Manda Agni*. *Ama* is the defined as toxic, pro-inflammatory waste product that blocks the body's channels, triggers negative immune reactions and considered to be a primary cause of internal disease.[4] The body may also produce *Ama* as a result of externally - manifested diseases.[4] Psychological distress also produces also produces a psychological form of *Ama* which manifests from misperception and disturbed emotions; giving rise to potentially harmful mental states such as anger, selfishness, and greed.[5] *Ama* is also regarded as the "Root cause of all diseases" and its elimination is one essential component of treatment.[4] The intestinal microbiota plays a major role in hosts physiological and pathological conditions. The microbiota consists of bacteria, archaea, Eucharica, viruses, fungi and bacteriophages colonizing in the GI tract. the key role of microbiota is digestion, metabolism, immune & environmental functions. This composition of microorganisms can be influenced by different environmental factor, lifestyle factors, food intake, stress, genetic vulnerability, medication, geography, age, gender throughout lifetime. This Gut microbial alteration is also known as Dysbiosis, a condition associated not only with gastrointestinal disorders and also metabolic disease like obesity & diabetes, autoimmune disorders, allergies, and mental health issues such as depression and anxiety. recently, it became evident that the intestinal bacteria can affect the central nervous system (CNS) physiology and inflammation. the gut -brain axis is the two-way biochemical signalling that takes place between the gastrointestinal tract (GI tract) and the central nervous system (CNS).[6]

## Structural Understanding of The *Agni* and Gut – Brain Axis

*Agni* is corelated as digestive fire which is responsible for all metabolic functions of the body. *Agni* is located in the *Grahani* according to all *Acharya*. *Grahani* as the word can be understand in the 3 different ways, as an anatomical structure, *Grahani Dosh*, *Grahani roga*. while understanding the role of *Grahani* in *Pachanakriya* we take *Grahani* as an anatomical structure. According to *Shabdakalpadhruma* *Grahani* defined as *Agnyaadhithana Nadi*[7] referring to tubular structure. according to *Acharya Sushruta* and *Vagbhata* it located in between the *Amashaya* and *Pakwashaya* from this reference we can co-relate gastro-intestinal tract. the layers of gastrointestinal tract are mucosa, sub mucosa, circular muscle layer and longitudinal muscle layer. in submucosa and mucosa layer 100 trillion of the microorganism are present. the gut microbiota is collection of bacteria, archaea, Eucharica, fungi & viruses which help in digestion of food. gut- brain axis is the bidirectional link between the CNS &ENS of body. ENS is web of sensory neurons, motor neurons and interneurons embedded in wall of gastrointestinal tract. stretching from lower third of the oesophagus right through to rectum. gut brain axis interaction occurs between endocrine (hypothalamic-pituitary-adrenal axis), immune (cytokines, chemokines) and the autonomic nervous system.[8]

## Functional Understanding of *Agni* and Gut Microbiota

- Microbiota maintain the integrity of the mucosal barrier. Microbiota provide the nutrients vitamin, metabolites, neuroactive substance, gut hormones & short chain fatty acids. Among that major short chain fatty acids are Butyrate, acetate, propionate. Butyrate main energy source of human colonocytes, play crucial role of homeostasis through B-oxidation, generating a state of hypoxia that maintains oxygen balance in the gut preventing gut microbiota dysbiosis, Intestinal gluconeogenesis these functions similar to the functions of *Agni* - *Aarogyam*
- Microbiota ferment and digest the food. Among the major short chain fatty acid Acetate play a role in central appetite regulation this function can be co-relate to the function of *Agni* that is *Tejas* Microbiota help in induction training,

- modulating & regulating the local immunity, systemic innate and adaptive response. The short chain fatty acid work on the immune system decreases the inflammation this function similar to the one of the functions of the *Agni* that describe as *Bala* and *Ojas*

## Discussion

### Role of *Agni* in Gut-Brain Axis

The bidirectional nature of the gut-brain axis plays a crucial role in maintaining overall health. However, factors such as consuming incompatible foods (*Viruddhaahara*), irregular eating habits (*Vishamashana*), and poor lifestyle choices can disrupt digestive fire (*Agni*). This disruption leads to an imbalance of *Doshas* and *Dhatu*s, ultimately resulting in disease. The intake of processed foods, sugar, and a sedentary lifestyle can alter gut microbiota, reducing its diversity and leading to a condition known as dysbiosis. Interestingly, gut lining microbiota can be compared to *Agni*, as both play a crucial role in food digestion. Dysbiosis can be seen as a state of *Agni Dusti* (digestive impairment). Not only physical factors but also mental and emotional states (*Manasika bhava*) can cause *Agni Dusti*, potentially leading to pathology. 90% of serotonin produce in gut any alteration in gut microbiome produces neurological disease like depression etc. The role of mental factors in disrupting *Agni* has been emphasized by ancient Ayurvedic scholars. According to *Madhava Nidana*, certain mental factors such as

- *Irshya* (jealousy)
- *Bhaya* (fear)
- *Krodha* (anger)
- *Lubdha* (confusion)
- *Ruk nipidita* (physical pain)
- *Dainya nipidita* (depression)
- *Pradvesha yukta* (food aversion)[9]

Even if wholesome foods are consumed in moderation, they may not be properly digested if an individual is experiencing:

- *Chinta* (worry)
- *Shoka* (grief)
- *Bhaya* (fear)
- *Krodha* (anger)

These mental factors directly affect *Agni*, leading to impaired digestion and potentially causing dysbiosis. For instance, excessive anger (*Atikrodhita*) can disrupt *Pitta Dosh*a, leading to improper digestion and contributing to the development of nervous system disorders. In addition to mental factors, lifestyle choices, such as staying up late (*Ratrijagrana*), can also disrupt *Agni*. This can lead to an imbalance of *Vata Dosh*a, causing digestive issues, dysbiosis, and potentially contributing to mental health disorders. The gut-brain axis plays a crucial role in various diseases, where the gut affects the brain and vice versa connection between the brain and gut through the Vagus nerve. when stressed the vagus nerve stimulated. HPA axis releases the cortisol releasing hormone (CRH). this will act on the immunocytes - immunocytes releases the peptide from the mast cell & other cell- this will cause the destruction in the gut lining - alteration in the gut microbiota - Dysbiosis (*Agnidusti*)

### *Ama* and Microbial endotoxins in production of the diseases

According to *Sushruta*, a disease is produced in six steps viz. *Sancaya*, *Prakopa*, *Prasara*, *Sthanasamsrya Vyakti* and *Bhedadvstha*. [10] In case of diseases produced by *Ama*, *Sancaya* of *Ama* is first step. It happens due to impairment of *Agni* at that place. Similar is the case with alteration in gut lining by microbiomes. Dysbiosis causes the release of metabolites (endotoxin) such as the lipopolysaccharides (LPS). Due to the thinning of the gut lining LPS release into the blood stream causes several diseases. When this *Sancaya* or accumulation is in small amount it does not cause any harmful effects, but if treatment is not given, this *Sancaya* exceeds the threshold. Then it starts producing minimal symptoms, this is the state of *Prakopa*. After this state, *Ama* goes into circulation, same is the case with LPS. Now this *Ama* requires a site for creating disease in form of *Khavaigunya* [11], which should be considered as weakness in any body tissue where *Ama* may be *Sthanasamsrya*, or many adhere with this tissue or cells. In case of LPS endotoxin release from the gut lining firstly in liver causes the inflammation led to fatty liver, insulin resistance in the liver leading to type 2 diabetes mellitus, elevated inflammatory marker such as TNF & IL-6. LPS endotoxin when it crosses the BBB causes the inflammation in the astrocytes. LPS endotoxin may develops the depression.

Therefore, depending upon this site of *Khavaigunya* different diseases are produced in different manner from same root cause, i.e., *Ama* or LPS endotoxin. This is the stage of *Sthanasamsrya*. Now symptoms of diseases become clear. All pathologies described in modern science are from this stage. In modern science, stages earlier to this are rarely considered. After this stage, pathology at gross level becomes visible. If even at this stage the disease is not treated it leads to complications, which are described in Ayurvedic classics as *Updravas*. From above discussion, it becomes clear that the method of production of disease at its basic level is described in similar manner in modern as well as in *Ayurvedic* literature.

## Conclusion

The main factor concerned in the formation of *Ama* is *Mandagni* (Hypo function of digestive faculty of body). Dietetic indiscretion and emotional stresses contribute to the formation *Ama*. This may be impaired the effective functioning of Functioning of gut brain axis. *Ama* produces also due to alteration in gut micro biota leading to accumulation of byproduct of metabolites of microbiota. Here it is noteworthy that whenever there will be improper metabolism due to impaired functioning of *Agni* then only *Ama* will be formed. In modern parlance, *Ama* may be referred to be lipopolysaccharides which is produced due to the alteration in the gut microbiota. The entire discussion concludes that various similarities between *Agni* and gut-brain axis in terms of the structure, function & pathophysiology (*Ama* and metabolites in production of diseases).

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