

Agni, Ama and the Gut–Brain Axis: An Integrative Ayurvedic Perspective on Microbiome, Metabolism and Neuroinflammation

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Abstract: *Background: The Gut–Brain Axis is a bidirectional communication network connecting the gastrointestinal tract and central nervous system through neural, endocrine, immune and metabolic pathways. Increasing evidence indicates that gut microbiota and their metabolites influence intestinal barrier integrity, immune activity, metabolic homeostasis and brain function. Ayurveda provides a distinct physiological framework centred on Agni, while Ama represents a pathophysiological concept associated with impaired digestion and abnormal transformation. Contemporary microbiome research may provide a hypothesis-generating framework for integrative medicine.*

Objective: To explore the conceptual relationship between Agni, Ama and the Gut–Brain Axis and identify potential biological mechanisms and future research directions connecting Ayurvedic digestive physiology with contemporary microbiome, metabolic and neuro immunological research.

Materials and Methods: A narrative conceptual review was undertaken using classical Ayurvedic literature concerning Agni, Agni Dushti, Ama, Ahara Paka and Srotos dushti, together with contemporary biomedical literature concerning the Gut–Brain Axis. Evidence relating to short-chain fatty acids, tryptophan metabolites, bile-acid derivatives, intestinal barrier function, immune signalling, vagal pathways, the hypothalamic–pituitary–adrenal axis and neuroinflammation was studied. Conceptual similarities and differences between Ayurvedic and biomedical frameworks were critically analysed.

Results: Agni represents a broader Ayurvedic concept encompassing digestion, transformation and metabolic processing. Contemporary research demonstrates that gastrointestinal homeostasis is influenced by dietary substrates, microbiota, microbial metabolites, epithelial barrier function, immune signalling and neural communication. Short-chain fatty acids, tryptophan-derived metabolites and bile-acid derivatives are among the important mediators of gut–brain communication. These findings provide a potential conceptual interface between Agni and digestive-metabolic homeostasis and between Ama and pathological consequences of disturbed gastrointestinal physiology. However, Agni cannot presently be considered synonymous with the gut microbiome, nor can Ama be equated directly with dysbiosis, intestinal permeability, endotoxemia or inflammation.

Conclusion: The Agni–Ama framework may provide a useful Ayurvedic conceptual model for generating testable hypotheses concerning digestion, gut ecology, systemic inflammation and brain function. Future translational research should combine standardized Ayurvedic phenotyping with microbiome, metabolomic, immunological, intestinal-barrier and neuropsychological assessments..

Keywords: Agni; Ama; Ayurveda; gut–brain axis; gut microbiome; microbiota; microbial metabolites; neuroinflammation; metabolism.



I. INTRODUCTION

Ayurveda considers digestion and metabolic transformation fundamental to the maintenance of health. Among its central physiological concepts, *Agni* represents the processes responsible for transformation of ingested substances, while *Grahani* is described in relation to retention and appropriate processing of food. Classical Ayurvedic descriptions therefore place digestive function upstream of nourishment, strength and systemic physiological stability.

The Charaka Samhita describes the importance of *Agni* in relation to life, strength, health, nourishment and other physiological functions. The *Grahani Chikitsa* chapter further presents *Agni* as central to digestion, metabolism and tissue nourishment.

When digestion and transformation are impaired, Ayurveda describes the development of *Ama*, broadly referring to incompletely processed or improperly transformed material. Importantly, *Ama* is a classical Ayurvedic construct and should not automatically be equated with a single modern entity such as a toxin, inflammatory mediator or bacterial metabolite.

Modern biomedical science has similarly moved from viewing the intestine as primarily a digestive organ toward understanding it as a metabolically and immunologically active ecosystem. The gut microbiota contributes to nutrient processing, energy metabolism, epithelial homeostasis, immune maturation and production of biologically active metabolites.

The Gut–Brain Axis represents bidirectional communication between the gastrointestinal tract and central nervous system through neural, endocrine, immune and metabolic pathways. The vagus nerve, hypothalamic–pituitary–adrenal signalling, enteroendocrine mechanisms, immune mediators and microbiota-derived metabolites all participate in this communication.

Consequently, the contemporary Gut–Brain Axis provides an interesting biological context for examining the Ayurvedic proposition that disturbance of digestion can have consequences beyond the gastrointestinal tract.

II. MATERIALS AND METHODS

The present study was designed as a narrative, conceptual review integrating classical Ayurvedic literature with contemporary biomedical evidence related to the Gut–Brain Axis, gut microbiome, metabolism, and neuroinflammation. Classical Ayurvedic references concerning *Agni*, *Ama*, *Grahani*, digestion, metabolism and systemic health were reviewed from authoritative texts including *Charaka Samhita*, *Sushruta Samhita* and *Ashtanga Hridaya*, along with relevant commentaries and scholarly Ayurvedic literature. Contemporary scientific literature was searched using electronic databases including PubMed, PubMed Central, Google Scholar and other relevant academic sources. The search was conducted using combinations of keywords such as “*Agni*,” “*Ama*,” “*Grahani*,” “*Ayurveda*,” “gut microbiome,” “gut microbiota,” “microbial metabolites,” “short-chain fatty acids,” “Gut–Brain Axis,” “microbiome and neuroinflammation,” and “immune signalling.” Articles addressing the relationship between intestinal microorganisms, microbial metabolites, metabolic regulation, immune responses, gut–brain communication and neuroinflammatory mechanisms were considered for the contemporary component of the review. Preference was given to peer-reviewed original research, systematic and narrative reviews, and recent publications with established scientific relevance. Retrieved literature was critically examined and thematically synthesized under the major domains of *Agni* and digestion, *Ama* and impaired transformation, gut microbial ecology, microbial metabolism, gut–brain communication and neuroinflammation. The Ayurvedic concepts were interpreted in their classical context and were not considered equivalent to specific biomedical entities such as digestive enzymes, dysbiosis, toxins or inflammatory mediators. The available evidence was therefore used to identify areas of conceptual correspondence and potential biological hypotheses while maintaining the distinction between classical Ayurvedic constructs and experimentally established biomedical mechanisms. As this was a narrative review based on previously published literature and classical textual sources, no human or animal subjects were directly recruited and no primary clinical data were generated.



AGNI IN AYURVEDA

Classical Ayurvedic texts describe *Agni* in different functional and anatomical classifications. In the *Charaka Samitha*, 13 *Agnis* are described, comprising *Jatharagni*, five *Bhutagni* and seven *Dhatvagni*. *Agni* is one of the central physiological concepts of Ayurveda.

Contemporary descriptions of Ayurvedic physiology classify *Agni* into:

Jatharagni

Bhutagni

Dhatvagni

Jatharagni is associated primarily with digestion of food, while *Bhutagni* and *Dhatvagni* are described in relation to subsequent levels of transformation and tissue metabolism.

The *Charaka Samhita* associates normal *Agni* with factors including:

Longevity,
Strength,
Health,
Nourishment,
Complexion,
Enthusiasm,
Ojas,
Tejas and
physiological vitality.

Thus, *Agni* can be interpreted as a multilevel Ayurvedic model of transformation, rather than being restricted to one anatomical organ or one biochemical pathway.

III. TYPES OF AGNI AND METABOLIC INTERPRETATION

TYPES OF AGNI

Ayurvedic concept	Classical functional description	Possible contemporary area
<i>Jatharagni</i>	Primary digestion	Gastric, pancreatic, intestinal digestive processes
<i>Bhutagni</i>	Transformation of elemental components	Nutrient processing and biochemical transformation
<i>Dhatvagni</i>	Tissue-level transformation	Cellular metabolism and tissue-specific metabolic pathways

STAGES OF AGNI

Ayurveda describes four functional states of *Agni*: *Samagni*, *Vishamagni*, *Tikshnagni* and *Mandagni*. These descriptions concern the qualitative and functional status of digestion.

Ayurvedic concept	Classical functional description	Possible contemporary area
<i>Samagni</i>	Balanced digestive function	Physiological digestive/metabolic homeostasis
<i>Vishamagni</i>	Irregular digestive function	Variable gastrointestinal function; requires empirical correlation
<i>Tikshnagni</i>	Excessively intense digestion	Hypermetabolic/hypercatabolic states as a research hypothesis
<i>Mandagni</i>	Diminished digestion	Impaired digestive/metabolic function as a research hypothesis

These relationships are hypotheses and are not established microbiome biomarkers of *Agni* states.



AMA: AYURVEDIC CONCEPT

Ama is described in Ayurveda in association with incomplete or abnormal digestion and transformation.

The Charaka tradition describes impaired *Agni* as an important factor in abnormal digestion and the formation of improperly transformed products.

Ama may therefore be understood within its classical context as a pathophysiological state/product associated with incomplete processing.

Importantly, *Ama* should not be simplistically translated as:

Bacterial toxin,

Endotoxin,

Inflammatory cytokine,

Free radical,

Undigested food,

Modern research may provide several biological phenomena that can be investigated alongside the *Ama* concept, including:

Altered intestinal permeability,

Microbial dysbiosis,

Abnormal microbial metabolites,

Metabolic disturbances,

Immune activation,

Chronic low-grade inflammation.

Ama-related Ayurvedic domain	Contemporary phenomenon that may be investigated	Evidence status
Impaired transformation	Altered metabolic processing	Hypothesis
Disturbed internal milieu	Changes in intestinal barrier or signalling	Conceptual correspondence
Systemic pathological consequences	Immune and inflammatory signalling	Biologically plausible research area
Altered microbial environment	Changes in microbial composition/function or metabolites	Research hypothesis

IV. THE GUT BRAIN AXIS

Gut–Brain Axis: Contemporary and Ayurvedic Perspective

The gut–brain axis (GBA) is a complex, bidirectional communication network linking the gastrointestinal tract and the central nervous system. It integrates the central nervous system (CNS), enteric nervous system (ENS), autonomic nervous system (ANS), neuroendocrine and immune pathways, hypothalamic–pituitary–adrenal (HPA) axis, and gut microbiota. Through neural, hormonal, immune and metabolic signals, this network contributes to gastrointestinal function, metabolic regulation, stress responses, behaviour and overall homeostasis.

The gut microbiota comprises the diverse microorganisms inhabiting the gastrointestinal tract. These microorganisms participate in the production and modulation of several biologically active compounds, including neurotransmitter-related substances such as serotonin, γ -aminobutyric acid (GABA), dopamine/catecholamines, acetylcholine and histamine. Microbial metabolites can influence intestinal motility, visceral sensation, immune activity and brain function. Dietary substrates are also metabolized by intestinal bacteria into short-chain fatty acids (SCFAs), which can enter systemic circulation and influence neuroimmune and metabolic processes. Alterations in microbial composition (dysbiosis) have been associated with changes in inflammatory mediators and signalling pathways involved in neurological and psychological functions.



Neural communication between the intestine and brain occurs substantially through the vagus nerve, while microbial metabolites and immune mediators provide additional routes of communication. Gut microbial activity may also influence processes related to neuroplasticity, including pathways involving brain-derived neurotrophic factor (BDNF) and synaptic proteins. Thus, the intestinal microbiome represents an important component of the physiological network maintaining gut and brain homeostasis.

Therefore, the gut–brain axis offers a biologically relevant context in which the Ayurvedic proposition that disturbances in digestion may have consequences beyond the gastrointestinal tract can be investigated, without presuming that the two frameworks are identical.

GUT MICROBES AND *AGNI*

Gut microbes play an important role in digestion, nutrient transformation, energy metabolism, immune regulation, and maintenance of intestinal homeostasis. In Ayurveda, these functions may be discussed conceptually through *Agni*, the principle responsible for digestion and metabolic transformation. A balanced *Agni* is associated with proper digestion, assimilation, and nourishment, whereas impaired *Agni* (*Agni Dushti*) may be considered in relation to disturbed digestive function and metabolic imbalance. Contemporary evidence suggests that dietary substrates are metabolized by gut microorganisms into bioactive compounds such as short-chain fatty acids, bile-acid derivatives, and tryptophan metabolites, which influence host metabolism, intestinal barrier integrity, immune responses, and gut–brain signalling. Thus, the interaction between *Agni*, diet, gut microbiota, and host metabolism provides a useful integrative framework for understanding how digestive function may influence systemic health. However, *Agni* should be regarded as an Ayurvedic functional concept rather than equated directly with the gut microbiome or any single physiological process.

MICROBIOME AND METABOLISM

The gut microbiome plays a significant role in host metabolism by contributing to the digestion and transformation of dietary components that are incompletely processed by human enzymes. Gut microorganisms ferment dietary fibres and other substrates to produce bioactive metabolites, including short-chain fatty acids such as acetate, propionate, and butyrate, as well as bile-acid and tryptophan-derived metabolites. These microbial products influence intestinal barrier integrity, energy balance, glucose and lipid metabolism, immune regulation, and neuroendocrine signalling. Alterations in the composition and functional activity of the gut microbiome, commonly referred to as dysbiosis, may modify microbial metabolite production and contribute to metabolic and inflammatory disturbances. Thus, the microbiome functions as an important metabolic interface between diet, the gastrointestinal tract, and systemic physiology, providing a contemporary biological perspective for understanding the Ayurvedic concepts of *Agni*, digestion, and metabolic homeostasis.

Agni state	Potential microbial domain to investigate	Potential metabolic domain
<i>Samagni</i>	Microbial community stability and functional diversity	Nutrient utilization and metabolic homeostasis
<i>Mandagni</i>	Microbial functional changes and fermentation profile	Altered substrate processing and energy metabolism
<i>Tikshnagni</i>	Microbial activity in relation to substrate availability	Energy expenditure and metabolic stress pathways
<i>Vishamagni</i>	Temporal variability in microbial function	Variability in digestion and metabolic signalling

This table is a research framework, not a diagnostic mapping between *Agni* states.

V. MICROBIOME AND NEUROINFLAMMATION

The gut microbiome plays an important role in regulating neuroimmune communication through the gut–brain axis. Intestinal microorganisms produce biologically active metabolites, including short-chain fatty acids (SCFAs),



tryptophan-derived metabolites and bile-acid derivatives, which can influence intestinal barrier integrity, systemic immune responses and central nervous system signalling. Alterations in microbial composition or function may modify these metabolic pathways and contribute to increased inflammatory signalling. Microbiota-derived signals can also influence microglia, the resident immune cells of the central nervous system, thereby affecting their maturation and activation state. SCFAs, particularly acetate, propionate and butyrate, have been investigated as mediators connecting microbial metabolism with microglial and neuroimmune function.

From an Ayurvedic perspective, this emerging microbiome–brain relationship may provide a research framework for understanding Ama and systemic inflammatory processes, although Ama should not be considered equivalent to dysbiosis, endotoxin or any single inflammatory mediator. Impaired Agni may be hypothesized to influence the intestinal environment and microbial metabolism, while altered microbial metabolites and barrier function could subsequently affect immune and neural signalling.

Thus, a proposed pathway is

Agni disturbance → altered intestinal environment → microbial/metabolic alterations → immune signalling → microglial activation → neuroinflammatory responses.

This represents a conceptual hypothesis requiring experimental and clinical validation rather than an established biomedical equivalence.

VI. INTEGRATIVE CONCEPTUAL FRAMEWORK

The Ayurvedic and biomedical frameworks can be placed side by side without assuming identity. In Ayurveda, Ahara is processed through Agni, with subsequent nourishment and maintenance of physiological function. In contemporary physiology, dietary substrates are digested by host enzymes and further transformed by microbial communities, generating metabolites that interact with epithelial, immune, endocrine and neural systems.

The potential research interface can therefore be framed as:

Ayurvedic phenotype → measurable physiological phenotype → microbiome/metabolome/immune phenotype → clinical outcome. This approach allows classical concepts to generate testable hypotheses while retaining their original conceptual context.

Ayurvedic construct	Classical emphasis	Contemporary research domain	Interpretive status
<i>Agni</i>	Digestion and transformation	Digestive and metabolic physiology	Conceptual correspondence
<i>Jatharagni</i>	Primary digestive processing	GI digestion and absorption	Functional comparison
<i>Dhatvagni</i>	Tissue-level transformation	Cellular/tissue metabolism	Hypothesis
<i>Ama</i>	Abnormal/incomplete transformation	Multiple possible pathological processes	No single biomedical equivalent
<i>Grahani</i>	Retention and processing of food; linked with Agni	GI functional regulation	Conceptual comparison
<i>Sroto dushti</i>	Disturbed transport/channel function	Barrier and signalling dysfunction	Hypothesis

VII. RESULTS

The literature reviewed supports six broad observations.

First, classical Ayurvedic sources place Agni centrally in digestion, transformation, nourishment and maintenance of physiological function.



Second, impaired Agni is described in relation to abnormal processing and Ama, but Ama does not map onto one specific modern biomedical entity.

Third, contemporary literature identifies the gut microbiota as an important participant in host metabolism and intestinal homeostasis. Microbial fermentation and biotransformation generate metabolites that interact with epithelial, immune, endocrine and neural systems.

Fourth, SCFAs, tryptophan-derived metabolites and bile-acid derivatives represent important molecular classes through which microbiota may influence host physiology.

Fifth, gut–brain communication involves multiple pathways rather than a single mechanism. Vagal signalling, immune mediators, endocrine pathways and circulating microbial metabolites may operate together.

Sixth, evidence for microbiome involvement in neuroinflammation is biologically compelling but heterogeneous, and causal inference in humans remains incomplete.

Taken together, the literature supports a conceptual research interface between Ayurvedic digestive physiology and contemporary gut–brain research. It does not establish direct equivalence between Agni and microbiome function or between Ama and dysbiosis, endotoxaemia, intestinal permeability or neuroinflammation.

VIII. DISCUSSION

The principal contribution of this narrative review is to frame Agni and Ama as hypothesis-generating Ayurvedic constructs that can be investigated alongside measurable biological systems. Agni is broader than digestion alone because classical descriptions encompass transformation and nourishment. Contemporary microbiome science likewise demonstrates that digestion extends beyond host enzymes to interactions among dietary substrates, microorganisms, metabolites and host tissues.

This conceptual overlap should nevertheless be interpreted carefully. Modern microbiome research measures microbial taxa, genes, metabolic pathways and metabolites, whereas Agni is assessed within an Ayurvedic clinical framework. A correlation between an Agni phenotype and a microbial or metabolic parameter would therefore represent an empirical association, not proof that the measured parameter is Agni itself.

A similar distinction is required for Ama. The classical concept may encompass a pattern of impaired processing and pathological consequence, while modern biomedical findings may include altered barrier function, microbial metabolites, immune activation or metabolic disturbance. Because several different biological processes could occur in the same clinical context, no single biomarker can presently be designated as the equivalent of Ama.

The gut–brain axis provides a useful interdisciplinary context because it integrates digestion, metabolism, immune signalling and neural communication. Contemporary reviews indicate that microbial metabolites and immune–neural pathways can influence brain-related physiology, while recent work continues to explore their role in neuroinflammatory and neuropsychiatric conditions.^{11–15} Nevertheless, observed microbiome differences are not necessarily causal, and effects identified in animal or experimental systems cannot automatically be generalized to human disease.

From an Ayurvedic research perspective, this creates an opportunity to operationalize classical concepts rather than redefine them. Future studies can prospectively classify participants using standardized Agni and Ama assessment tools and then examine whether those phenotypes correlate with dietary patterns, gastrointestinal symptoms, microbial community structure, microbial metabolites, intestinal-barrier markers, inflammatory mediators and validated neuropsychological outcomes.

Such studies should be designed to account for major microbiome confounders including diet, medication exposure, antibiotics, age, sex, lifestyle, sleep, geography and metabolic status. Repeated sampling may also be necessary because the microbiome and metabolome are dynamic rather than fixed characteristics.

The conceptual model proposed in this review should therefore be regarded as a bridge for research rather than a completed mechanistic theory. Its value will ultimately depend on whether the proposed Ayurvedic phenotypes can be standardized, reproduced and related to objectively measurable biological and clinical outcomes.



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