From Agni to The Microbiota-Gut-Brain Axis: A Critical Translational Framework for *Grahanidosha, Irritable Bowel Syndrome, And Priyangvadi Basti*

Dr. Fatemeh Moazzamipeiro[1], Nisha Gupta[2], Gopesh Mangal[3]
[1]*PG Scholar, Department of Samhita and Maulik Siddhant, National Institute of Ayurveda (Deemed University), Jaipur, Raj*
[2]*Professor and HOD, Department of Samhita and Maulik Siddhant, National Institute of Ayurveda (Deemed University), Jaipur, Raj*
[3]*Professor and HOD, Department of Panchakarma, National Institute of Ayurveda (Deemed University), Jaipur, Raj*

***Abstract*—irritable bowel syndrome (IBS) is a heterogeneous disorder of gut-brain interaction characterized by recurrent abdominal pain or discomfort and altered bowel habits without structural disease sufficient to explain the full symptom complex. Its pathophysiology may include variable combinations of motility disturbance, visceral hypersensitivity, altered central processing, epithelial barrier dysfunction, mucosal immune activation, dietary fermentation, microbial ecological disturbance, metabolite variation, autonomic dysregulation, and psychosocial influences. Ayurveda describes Grahanidosha as a chronic digestive regulatory disorder centered on impaired *Agni*, defective retention and progression of food, incomplete transformation, *Ama* formation, and *Vata*-mediated instability. This critical narrative review examines classical descriptions from the *Charaka Samhita*, *Sushruta Samhita*, and *Ashtanga Hridaya* alongside contemporary evidence on IBS, microbiota, intestinal interface biology, neuroimmune signaling, post-infective change, psychophysiological regulation, and the microbiota-gut-brain axis. A five-layer translational model is proposed, linking transformation, substrate ecology, digestive interface integrity, coordinated movement, and central-affective regulation while preserving essential boundaries: *Grahanidosha* is not identical to IBS; *Ama* is not synonymous with dysbiosis; *Pittadhara Kala* is not equivalent to intestinal mucosa; and *Vata* cannot be reduced to neural control. *Priyangvadi Basti* is interpreted as a classical *Grahi* and *Vata*-regulating intervention whose clinical efficacy and biomedical mechanisms require direct testing. The framework is intended to support reproducible Ayurvedic phenotyping, standardized intervention protocols, validated patient-centered outcomes, and prespecified mechanistic research rather than retrospective claims of equivalence.**

***Index Terms*—Grahani; Agni; Ama; Irritable Bowel Syndrome; Gut-Brain Axis; microbiota; Basti**

I. INTRODUCTION

Irritable bowel syndrome (IBS) is a prevalent chronic disorder of gut-brain interaction in which recurrent abdominal pain or discomfort occurs with altered stool frequency, stool form, defecation, or a combination of these features. Contemporary diagnostic systems favor a positive symptom-based diagnosis supported by limited testing guided by age, alarm features, bowel phenotype, and clinical context rather than indiscriminate exclusion of every organic disorder. Rome IV formalized IBS as a disorder of gut-brain interaction, while the Rome V process published in 2026 further separates clinical from research criteria and broadens the clinical construct by reintroducing discomfort alongside pain. Much of the existing epidemiologic and therapeutic literature, however, remains based on Rome III or Rome IV populations. [1-5]

The public-health significance of this subject extends beyond symptom prevalence. The Rome Foundation global epidemiology study documented a substantial worldwide burden of disorders of gut-brain interaction, together with impaired quality of life and

increased health-care use. Prevalence estimates vary according to the criteria, sampling method, culture, and survey mode; therefore, a single number should not be treated as universal. Nevertheless, IBS remains one of the conditions most frequently encountered in primary and specialist gastroenterology, and it can affect work, food choice, travel, social confidence, sleep, intimate relationships, and repeated health-seeking behavior. Clinical guidelines consequently emphasize a constructive diagnosis, explanation of the disorder, continuity of care, and a therapeutic relationship that validates symptoms without implying destructive bowel disease. [6,7]

IBS is clinically and biologically heterogeneous. Patients may have diarrhea-predominant, constipation-predominant, mixed, or unclassified bowel patterns, and individuals can shift between subtypes over time. Symptom severity is influenced not only by transit and stool consistency but also by visceral sensitivity, central appraisal of afferent signals, dietary fermentation, bile acid physiology, epithelial permeability, mucosal immune activity, microbiota composition and function, autonomic regulation, sleep, anxiety, stress, and prior gastrointestinal infection. No single abnormality is present in all patients, and no single biomarker currently defines the disorder. This heterogeneity explains why symptom-targeted therapies may help selected patients yet produce inconsistent results across broader populations. [1,4,5,8]

This heterogeneity has an important consequence for translational research: the label IBS identifies a clinical syndrome, not one uniform biological pathway. A diarrhea-predominant patient with prior infectious enteritis, urgency, increased permeability, and anxiety may differ substantially from a constipation-predominant patient with slow transit, pelvic-floor dysfunction, and food-related bloating. Even within a bowel subtype, microbial composition, metabolite production, visceral sensitivity, diet, bile-acid handling, immune activity, and coping patterns may diverge. Mechanistic studies that pool these phenotypes can generate contradictory averages, while small subgroup studies can overstate unstable signals. A rigorous Ayurveda-biomedicine comparison must therefore begin with phenotype, stage, and context rather than assuming that every patient carrying the same modern diagnosis has the same *Grahani Samprapti*. [7,9,10]

The classical Ayurvedic account of *Grahanidosha*(chronic digestive regulatory disorder) arises from a different conceptual and diagnostic system. *Grahani* is closely related to *Agni* (digestive-metabolic transformative capacity), and its physiological role includes holding ingested food during digestion, supporting transformation, and permitting onward movement after appropriate processing. When *Agni* becomes weak, irregular, or otherwise disturbed, retention and transformation become defective, incompletely processed material may pass onward, stool pattern becomes unstable, appetite and strength decline, and chronic digestive symptoms may develop. The pathology is therefore organized around transformation, containment, timing, movement, and the interaction of *Agni* with *Pachaka Pitta*, *Samana Vata*, *Apana Vata*, and *Pittadhara Kala*. [11-13]

Modern comparative writing frequently weakens this subject by imposing direct identities such as *Grahani* equals the duodenum, *Ama* equals toxin or dysbiosis, *Pittadhara Kala* equals intestinal mucosa, or *Vata* equals the enteric nervous system. These equations are neither textually secure nor scientifically necessary. Ayurvedic constructs integrate functions that biomedicine distributes among several anatomical, biochemical, neural, endocrine, immune, and ecological systems. A more defensible method is to compare regulatory patterns while maintaining the difference between the two knowledge systems. Both *Grahanidosha* and IBS can then be examined as conditions in which clinically important symptoms arise from unstable coordination rather than a single gross structural lesion.

The present review develops a critical translational framework linking classical *Grahani* physiology and pathogenesis with selected evidence concerning IBS, the microbiota-gut-brain axis, barrier physiology, neuroimmune activity, visceral hypersensitivity, and psychophysiological regulation. It also examines the classical rationale of *Priyangvadi Basti* in the context of *Grahi Basti* and *Vata*-oriented treatment. The purpose is not to declare diagnostic or mechanistic identity, but to identify coherent, testable questions for integrative gastroenterology while preventing unsupported retrospective claims.

II. OBJECTIVES

The objectives of this review were: (1) to examine the classical understanding of *Grahanidosha* with particular reference to *Agni*, *Ama*, *Pachaka Pitta*, *Samana Vata*, *Apana Vata*, and *Pittadhara Kala*; (2) to summarize selected contemporary mechanisms implicated in IBS, including motility disturbance, visceral hypersensitivity, microbial alteration, epithelial barrier dysfunction, immune activation, autonomic imbalance, and psychosocial regulation; (3) to compare the two frameworks without proposing direct equivalence; and (4) to evaluate the classical rationale and research potential of *Priyangvadi Basti* in chronic bowel instability.

III. MATERIAL AND METHODS

This article was developed as a narrative and translational review. The author's extended source manuscript was reorganized using a predefined framework separating classical Ayurvedic physiology, contemporary IBS evidence, critical comparison, therapeutic rationale, and research implications. Classical material was drawn from *Grahani*-related descriptions in the *Charaka Samhita*, the account of *Pittadhara Kala* and *Grahi Basti* in the *Sushruta Samhita*, and the *Grahani* discussion in the *Ashtanga Hridaya*. Because wording, pagination, and verse numbering vary among editions and commentaries, the editor, edition, chapter, verse, and page number of every classical citation must be checked against the physical books actually used by the author before publication.

A focused biomedical search was conducted using PubMed, the Rome Foundation website, major gastroenterology guideline repositories, journal publisher sites, and reference lists of authoritative reviews. Search combinations included: ("irritable bowel syndrome" OR IBS) AND ("gut-brain axis" OR "disorder of gut-brain interaction"); ("irritable bowel syndrome" OR IBS) AND (microbiota OR microbiome OR dysbiosis); ("irritable bowel syndrome" OR IBS) AND ("intestinal permeability" OR barrier OR neuroimmune); IBS AND visceral hypersensitivity; IBS AND autonomic regulation; post-infection AND irritable bowel syndrome; Ayurveda AND *Grahani*; *Agni* AND *Grahanidosha* ; and *Basti* AND *Grahani*. Bibliographic details were cross-checked through DOI and PubMed records where available.

English-language consensus statements, clinical guidelines, systematic reviews, meta-analyses, major narrative reviews, and clinically relevant mechanistic studies were considered when they directly addressed IBS definition, diagnostic framing, motility, visceral sensation, microbiota, barrier physiology, immune activity, stress, autonomic regulation, or post-infectious disease. Classical sources were included when they directly informed *Grahani*, *Agni*, *Ama*, *Vata*, *Pittadhara Kala*, *Grahi* therapy, or *Basti*. Sources were excluded when they lacked traceable bibliographic information, were unrelated to the defined domains, or asserted Ayurvedic-biomedical equivalence without textual or empirical support.

The synthesis followed three methodological rules. First, Ayurvedic concepts were defined from their own textual functions before a modern comparison was introduced. Second, biomedical mechanisms were treated as possible domains of dialogue rather than translations of Sanskrit terminology. Third, classical indication, contemporary plausibility, and demonstrated clinical mechanism were kept separate. Accordingly, proposed relationships between *Priyangvadi Basti* and motility, microbiota, epithelial, immune, autonomic, or neural outcomes are presented as research hypotheses rather than established effects. Because this was a narrative review, no pooled analysis, formal risk-of-bias assessment, or certainty grading was performed.

Classical interpretation used functional triangulation rather than isolated quotation. A concept was included only when its meaning could be situated within the relation among digestive transformation, retention, movement, stool characteristics, appetite, strength, and therapeutic reasoning. Etymology was treated as supportive rather than decisive, and commentarial or anatomical interpretations were not used to erase the broader physiological function of the term. Modern evidence was weighted hierarchically: consensus documents and clinical guidelines informed definitions and clinical framing; systematic reviews and meta-analyses informed the consistency of associations or treatment effects; major mechanistic studies were used to illustrate biological plausibility; and preclinical findings were explicitly separated from demonstrated human mechanisms. This method does not create equivalence between knowledge systems. It

identifies where two frameworks describe comparable regulatory problems, where they remain incommensurable, and which proposed bridges are sufficiently precise to test.

IV. CLASSICAL UNDERSTANDING OF GRAHANIDOSHA

The term *Grahani* is derived from the verbal root grah, indicating holding, receiving, or retaining. In the digestive context, it denotes a function that retains ingested material until digestion has reached an appropriate stage. The *Charaka Samhita* identifies *Grahani* as the seat of *Agni* and describes their mutual dependence: competent *Agni* supports appropriate retention, digestion, and release, whereas impaired *Agni* weakens the retaining function and permits inadequately processed material to pass onward. [11]

Grahani is best understood as a relational physiological construct. Its identity is not established by location alone, but by what it accomplishes in association with *Agni*: it receives food after ingestion, sustains an appropriate period of digestive processing, supports transformation, and permits onward movement when the material is sufficiently processed. The same construct therefore includes temporal control, containment, transformation, discrimination, and release. A direct anatomical equation with the pylorus, duodenum, proximal small intestine, or a single mucosal layer captures only fragments of this function. The classical description is closer to an organized digestive checkpoint distributed across several interacting functions than to an isolated organ in the modern anatomical sense. [11-13]

This account is primarily functional rather than narrowly anatomical. The region between *Ama*shaya and Pakvashaya is relevant to the classical description, and some modern authors correlate *Grahani* with the duodenum or proximal small intestine. Nevertheless, the attributed activities include timing, containment, transformation, separation, and regulated progression. These processes require coordination across more than one modern anatomical structure. *Grahani* is therefore more accurately discussed as a digestive regulatory organ-function complex than as a one-to-one synonym for a single segment of bowel.

In the classical pathogenic sequence, exposure to unsuitable food, irregular eating, overeating, fasting beyond capacity, incompatible combinations, unresolved diarrheal illness, emotional disturbance, or other *Dosha*-provoking factors impairs *Agni*. Food is then processed incompletely or at an inappropriate rate. The disturbed system may release material prematurely, retain it abnormally, or alternate between these patterns. Repeated disturbance establishes chronic instability in appetite, digestion, bowel form, frequency, postprandial comfort, and strength. This process constitutes more than simple diarrhea: it is a failure of coordinated digestion and evacuation.

The clinical grammar of *Grahanidosha* is similarly multidimensional. Stool may be loose, unformed, frequent, delayed, hard, mixed, or alternating according to *Dosha* predominance, *Agni* pattern, stage, diet, and the degree of *Ama*. Appetite can be reduced, irregular, excessive yet ineffective, or associated with postprandial discomfort. Patients may report abdominal heaviness, distension, gurgling, pain, sour or abnormal eructation, fatigue, loss of strength, and dissatisfaction after defecation. These features matter because they prevent the disease from being reduced to diarrhea alone. They also show that stool is interpreted as an output of a larger digestive process. The clinically meaningful question is not simply how often evacuation occurs, but whether food is transformed, retained, assimilated, and eliminated in an orderly manner. [11,13]

Clinical descriptions of *Grahanidosha* include irregular appetite, abdominal discomfort, bloating, borborygmi, weakness, altered taste, excessive thirst in selected patterns, and stools that may be loose, formed, hard, mixed, or incompletely processed according to the dominant *Dosha*, stage, and condition of *Agni*. The apparent contradiction between loose and retained bowel patterns is therefore not a defect in the classical category; it reflects the instability of the underlying regulatory process. This feature is particularly relevant when considering chronic bowel disorders with fluctuating phenotypes.

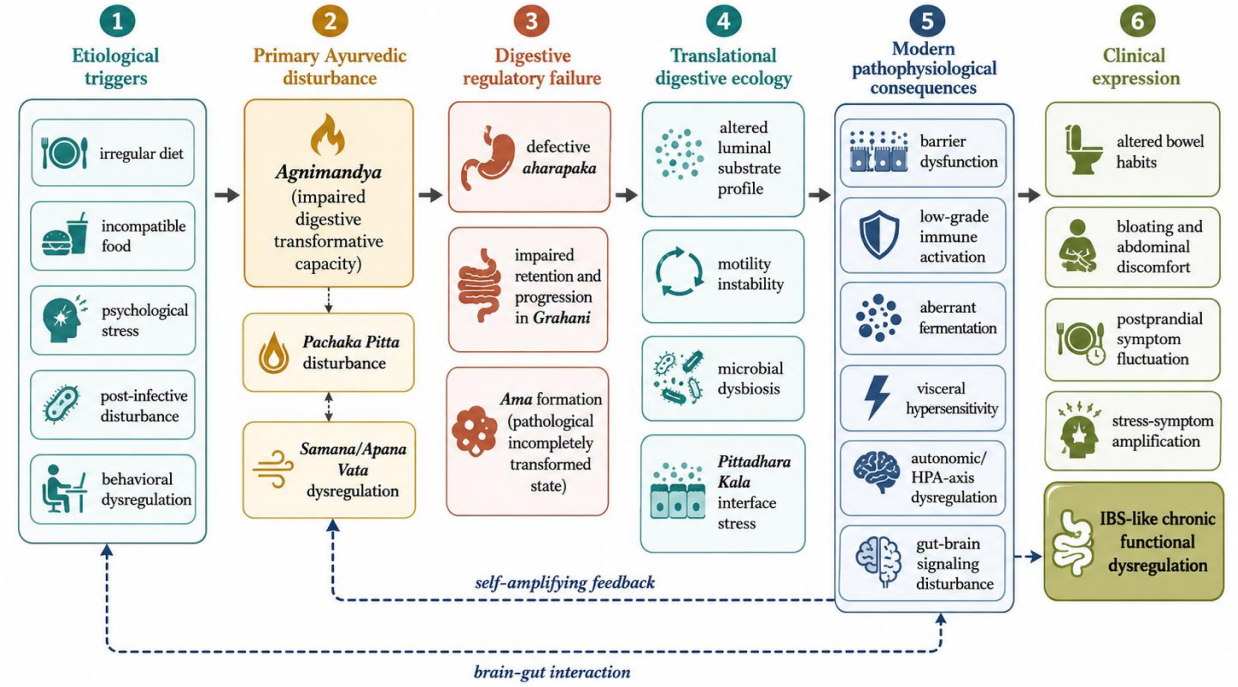
The classical relation between *Atisara* (diarrheal disease) and subsequent *Grahanidosha* also deserves attention. The texts recognize that premature or incomplete return to normal food and activity after diarrhea can perpetuate weakness of *Agni* and produce a chronic pattern. The modern concept of post-infectious IBS cannot be retrospectively assigned to this account, but both frameworks recognize that an acute intestinal event may be followed by prolonged

digestive dysregulation after the initiating episode has resolved.

The classical transition from *Atisara* to *Grahanidosha* is especially relevant to chronicity. Repeated or incompletely resolved diarrheal illness can leave digestion weak even after the acute episode has settled. If ordinary or heavy food is resumed before *Agni* recovers, the digestive system may remain vulnerable to recurrent looseness, irregular appetite, and incomplete processing. This sequence should not be declared identical to post-infectious IBS, because the classical diagnosis, causal vocabulary, and required exclusions are different. It nevertheless provides a clinically recognizable pattern: an acute intestinal disturbance is followed by incomplete functional recovery and a persistent disorder of bowel regulation. This temporal architecture is one of the strongest grounds for a cautious comparison with modern post-infective disease. [11,14,15]

Accordingly, *Grahanidosha* is best understood as an *Agni*-centered syndrome of impaired transformation, defective retention, disordered progression, and chronic digestive instability. This definition is broad enough to preserve classical meaning while remaining sufficiently precise for critical comparison with modern disorders of gut-brain interaction.

Figure 1. Integrated pathophysiology of *Grahani Roga* and IBS-like gut-brain dysfunction



Conceptual translational model; not a claim of direct one-to-one equivalence between Ayurvedic and biomedical entities.

V. AGNI, AMA, VATA, PACHAKA PITTA, AND PITTADHARA KALA AS DIGESTIVE REGULATORY CONCEPTS

Agni is the central organizing principle of the classical model. Although frequently translated as digestive fire, its physiological scope extends beyond heat or a single secretion. At the gastrointestinal level, *Jatharagni* denotes the capacity to transform food into material suitable for absorption, tissue nourishment, and further metabolism. Its function therefore includes the adequacy, timing, and completeness of digestion. The wider hierarchy of *Bhutagni* and *Dhatvagni* extends transformation beyond the lumen, but *Grahanidosha* is primarily rooted in disturbance of *Jatharagni*. A scientifically cautious translation is digestive-metabolic transformative capacity rather than gastric acid, enzymes, or energy expenditure alone.

Pachaka Pitta is closely associated with digestive transformation. Classical descriptions attribute to it the processing of food and support of the other functional expressions of Pitta. A modern comparison may therefore consider the coordinated secretory and catalytic environment of digestion, including acid, enzymes, bile-associated processing, and chemical transformation. None of these elements, however, is individually equivalent to *Pachaka Pitta*. The concept remains a functional category within the Ayurvedic system rather than an unrecognized name for a modern molecule or organ.

The hierarchy of *Agni* further prevents digestive interpretation from being confined to the lumen. *Jatharagni* governs primary processing of ingested food, while *Bhutagni* and *Dhatvagni* extend transformation into elemental and tissue-level domains. These categories do not correspond one-to-one with enzymes, hepatic pathways, mitochondrial metabolism, or tissue biochemistry, yet they express a continuous principle: the biological value of food depends on successful transformation at successive levels. *Grahanidosha* is centered on *Jatharagni* because disturbance begins in primary digestion, but persistent impairment may affect nourishment, strength, and systemic function. The framework therefore links bowel symptoms with the quality of assimilation and tissue support without requiring the claim that every systemic symptom arises from one measurable gastrointestinal defect. [11]

Vata contributes movement, timing, coordination, and directional control. *Samana Vata* operates in the digestive region and is associated with receiving food, supporting digestion, separating useful and waste fractions, and coordinating progression. *Apana Vata* governs distal movement and evacuation. Disturbance may therefore appear as premature propulsion, delayed transit, alternating bowel behavior, urgency, incomplete evacuation, gaseous distension, or poorly coordinated defecation. Modern physiology locates related functions in smooth muscle, enteric and autonomic neural pathways, reflex circuits, endocrine signals, and luminal factors; *Samana Vata* and *Apana Vata* should not be reduced to any one of these components.

Ama emerges when transformation is inadequate. The term carries the sense of immaturity, incompleteness, or insufficient processing. In *Grahanidosha* , *Ama* may involve inadequately digested alimentary material and a broader pathological state in which the products of transformation are not physiologically appropriate. Translating *Ama* simply as toxin is misleading because it suggests a defined poisonous chemical entity. Equating it with endotoxemia, microbial overgrowth, or dysbiosis is equally unsupported. A more defensible interpretation is pathological incompleteness associated with altered substrate handling and an unfavorable digestive milieu.

Aharapaka and *Vipaka* provide a temporal dimension to this model. *Aharapaka* describes the progressive processing of food, whereas *Vipaka* concerns the consequential post-digestive effect through which the transformed substrate becomes physiologically meaningful. This distinction resembles neither a simple early-versus-late digestion scheme nor a direct map of specific biochemical stages. Its translational value lies in recognizing that digestion changes the nature of substrates delivered to distal bowel communities and to the host. Transit time, secretion, bile acids, nutrient absorption, and microbial metabolism together determine which molecules remain available, where fermentation occurs, and what metabolites contact the epithelium. Thus, incomplete transformation can be discussed as an altered substrate ecology without redefining *Ama* as a microorganism or metabolite. [16,17]

The digestive milieu is nevertheless relevant to modern ecological interpretation. Transit time, nutrient availability, bile acids, secretions, pH, oxygen gradients, medications, and diet influence microbial composition and metabolism. Incomplete or irregular processing can alter which substrates reach distal microbial communities and may modify fermentation, gas production, osmotic load, and metabolite profiles. Thus, *Ama* is not dysbiosis, but an *Ama*-producing digestive state may generate conditions in which microbial ecology and host-microbial signaling are altered. This proposition is plausible at a systems level and requires direct empirical testing.

Pittadhara Kala is described in the *Sushruta Samhita* as a digestive-supporting interface situated between proximal and distal alimentary regions. Kala is often translated as membrane, yet the classical usage conveys a structural-functional layer that supports containment and activity. A cautious modern comparison may therefore invoke digestive interface biology, encompassing the luminal-epithelial

boundary, mucus, secretory environment, immune surveillance, enteroendocrine signaling, and selective permeability. *Pittadhara Kala* is not identical to intestinal mucosa, but the comparison highlights the classical recognition that transformation depends on an organized interface and not only on luminal contents. [12]

These constructs form a coordinated model. *Agni* provides transformative competence; *Pachaka Pitta* represents the digestive-transformative environment; *Samana Vata* and *Apana Vata* coordinate movement, separation, and evacuation; *Pittadhara Kala* provides an interface for organized digestive activity; and *Ama* denotes pathological incompleteness when transformation fails. *Grahanidosha* develops when disruption in one domain propagates through the others, producing unstable feedback between digestion, movement, stool formation, and systemic strength. Table 1 summarizes the comparison boundaries.

Taken together, *Agni*, *Pachaka Pitta*, *Vata*, *Pittadhara Kala*, and *Ama* describe a nonlinear control problem. Transformation depends on a suitable environment and adequate time; time and contact depend on coordinated movement; the interface influences secretion, absorption, immune tolerance, and sensation; and the products of incomplete processing can further disturb movement and interface function. This circularity helps explain why chronic digestive disorders fluctuate rather than progress in a simple straight line. A stressful event, dietary change, infection, sleep loss, or inappropriate treatment may disturb one component and amplify the others. The model is therefore better represented by feedback loops than by a single chain of causation. Its scientific usefulness rests in generating testable domains while retaining the original Ayurvedic organization of disease.

Table 1. Classical Concepts And Cautious Translational Interpretation

Ayurvedic concept	Classical function	Possible comparison domain	Required caution
Grahani	Retention, transformation-linked containment, and regulated progression	Digestive regulatory organ-function complex	Not identical to the duodenum or one organ
Agni	Adequacy and completeness of digestive-metabolic transformation	Integrated digestive and metabolic capacity	Not identical to acid, enzymes, or caloric metabolism
Ama	Pathological incompleteness after defective transformation	Altered substrate handling and digestive milieu	Not identical to toxin, endotoxemia, or dysbiosis
Samana/Apana Vata	Coordination, movement, separation, and evacuation	Motility and neuroenteric-autonomic coordination	Not identical to the enteric or autonomic nervous system
Pittadhara Kala	Supportive interface for digestive transformation	Digestive interface and barrier biology	Not identical to intestinal mucosa
Basti	Classical therapy for Vata-mediated regulatory disturbance	Rectal intervention requiring clinical and mechanistic study	Modern systemic mechanisms remain unproven

VI. IBS, MICROBIOTA, BARRIER, AND THE GUT-BRAIN AXIS

Modern IBS research similarly rejects a single-lesion model. The disorder is defined clinically, but its biological expression is heterogeneous. Altered transit may dominate in one patient, visceral hypersensitivity in another, while dietary-luminal events, bile acid abnormalities, pelvic floor dysfunction, psychological distress, or post-infectious changes may be more important in others. These mechanisms interact rather than forming mutually exclusive subtypes. A patient with accelerated transit may also have heightened visceral perception, stress-related autonomic activation, and altered fermentation. [1,4,5,8,18]

Visceral hypersensitivity refers to enhanced perception or pain in response to physiological or experimental gastrointestinal stimuli. Peripheral sensitization may arise from epithelial, immune, microbial, or neural changes, while central amplification can alter the interpretation and salience of afferent input. The relationship is bidirectional: pain anticipation, hypervigilance, anxiety, and prior adverse experiences may increase symptom intensity, whereas repeated painful gut signals can strengthen central threat processing. The severity of perceived symptoms therefore cannot be inferred reliably from visible structural findings alone. [18,19]

Microbiome findings require particular methodological restraint. Studies differ in diagnostic criteria, bowel subtype, diet, medication exposure, geography, stool handling, DNA extraction, sequencing region, analytical pipeline, and whether fecal or mucosa-associated communities are sampled. Relative abundance data can also make one taxon appear increased because another has decreased. Systematic reviews have identified recurring differences in selected taxa and diversity measures, yet no universal microbial signature currently diagnoses IBS at the individual level. A recent reanalysis across multiple cohorts strengthened evidence for group-level compositional and predicted functional differences, but it also confirmed substantial heterogeneity and the need for multi-omic, phenotype-aware research. Microbiota should therefore be considered one variable component of IBS biology, not the single cause of the syndrome. [16,20,21]

The microbiota is one component of this network. Systematic reviews identify group-level differences between IBS and healthy controls, but findings vary by geography, diet, medication, sequencing method, stool phenotype, and analytic pipeline. No universal IBS microbial signature has been established. Relevant functions may include carbohydrate fermentation, gas production, short-chain fatty acid metabolism, bile acid transformation, proteolytic metabolites, immune education, epithelial signaling, and modulation of enteric or vagal pathways. Modern reviews therefore emphasize function and host-microbial interaction rather than treating dysbiosis as a single measurable lesion. [16,20,22]

Function may be more informative than taxonomy alone. Microorganisms transform carbohydrates, proteins, bile acids, and host-derived substrates into short-chain fatty acids, gases, indoles, phenolic compounds, and other signaling molecules. These products can alter luminal pH, epithelial metabolism, immune tone, motility, secretion, and sensory signaling. However, fecal metabolite concentration is an imperfect proxy for production because it also reflects absorption, transit, diet, and sampling. Meta-analyses of short-chain fatty acids and serotonin report heterogeneous and sometimes subtype-dependent findings; a statistically different group mean does not establish a stable biomarker or a causal pathway in every patient. Serotonin participates in motility, secretion, and sensory signaling, but peripheral concentration cannot be used as a simple measure of mood or central neurotransmission. [17,22,23]

Epithelial barrier dysfunction has been demonstrated in subsets of patients, particularly in some diarrhea-predominant and post-infectious phenotypes, but it is neither universal nor specific to IBS. Increased permeability can enhance exposure of mucosal immune cells and sensory nerves to luminal antigens and microbial products. Mast cells, cytokines, epithelial mediators, and local neural pathways may then contribute to pain, urgency, and altered secretion. Barrier change can be both cause and consequence: stress, infection, diet, bile acids, inflammation, and microbial metabolites may affect tight-junction regulation, while altered permeability can amplify neuroimmune signaling. [24,25]

The epithelial interface is another important but nonuniform domain. Increased permeability has been reported particularly in diarrhea-predominant and post-infective subgroups, but methods and thresholds vary. Barrier integrity depends on epithelial cells,

tight-junction regulation, mucus, antimicrobial defenses, immune surveillance, vascular and neural influences, and microbial metabolites. Low-grade immune activation may amplify afferent signaling even without destructive inflammation. The observation that activated mast cells located near colonic nerve fibers correlate with abdominal pain in some patients illustrates a plausible neuroimmune bridge, but it should not be generalized to all IBS phenotypes. This evidence supports studying interface stress and neuroimmune sensitization; it does not justify relabeling IBS as a uniform inflammatory disease. [24-26]

The brain-gut component is equally important. Psychological factors do not imply that symptoms are imagined. Stress activates central, autonomic, and hypothalamic-pituitary-adrenal pathways that can modify motility, secretion, permeability, immune function, pain modulation, and microbial habitat. Conversely, persistent bowel symptoms can impair sleep, social function, mood, food-related confidence, and quality of life. Heart-rate variability studies support autonomic alteration in some cohorts, although effect sizes and direction vary. Contemporary brain-gut behavioral treatments, including cognitive behavioral approaches and gut-directed hypnotherapy, can improve abdominal pain in selected patients, supporting the clinical relevance of central-peripheral regulation. [27-29]

Diet operates simultaneously as nutrient exposure, sensory experience, osmotic load, fermentable substrate, and cultural behavior. Fermentable oligosaccharides, disaccharides, monosaccharides, and polyols can increase luminal water and gas in susceptible individuals, and controlled feeding studies support symptom reduction with a low-FODMAP diet in selected patients. Yet prolonged indiscriminate restriction may reduce dietary diversity, burden patients socially, and alter microbial substrates. The therapeutic principle is therefore structured restriction followed by reintroduction and personalization, ideally under qualified dietary guidance. This modern observation has a useful but limited dialogue with Ayurvedic attention to quantity, timing, compatibility, preparation, individual capacity, and postprandial response. The overlap lies in individualized dietary regulation, not in declaring FODMAP categories equivalent to classical *Guna* or *Virya*. [7,30]

Post-infectious IBS provides a particularly clear example of interacting mechanisms. After acute enteritis, a subgroup of patients develops persistent abdominal symptoms and altered bowel habits. Risk is influenced by the severity and duration of infection, sex, psychological factors, and possibly the nature of the pathogen and treatment. Proposed mechanisms include residual immune activation, epithelial changes, altered enteric signaling, microbial disruption, and central sensitization. The disease persists after the original infection has resolved because regulatory networks may remain altered. [14,15]

Microbiota-directed treatment further demonstrates the gap between plausibility and clinical proof. Probiotic meta-analyses include many strains, combinations, doses, durations, and outcomes; some preparations show benefit, but certainty is generally low and effects cannot be transferred automatically from one strain to another. Fecal microbiota transplantation can alter community composition, yet randomized trials and meta-analyses have produced inconsistent symptom outcomes, with donor, route, dose, placebo design, and follow-up influencing results. Conversely, transferring microbiota from selected patients with IBS into germ-free mice has reproduced aspects of altered transit, barrier function, and behavior, supporting possible causality in defined experimental settings. These findings establish the microbiome as biologically active while warning against the claim that changing microbiota necessarily cures IBS. [31-33]

These findings justify comparison with *Grahanidosha*at the level of network organization. Both frameworks recognize that bowel symptoms are influenced by transformation, timing, movement, interface integrity, emotional state, and prior digestive insult. Nevertheless, the modern categories are based on measurable biological processes and symptom criteria, whereas the Ayurvedic categories derive from *Dosha*, *Agni*, *Ama*, and *Samprapti*. Translational work is strongest when it converts this conceptual overlap into falsifiable questions rather than declaring historical equivalence.

Figure 2. Ayurvedic constructs and their translational comparison domains

Ayurvedic construct	Classical functional meaning	Translational comparison domain	Required interpretive caution
1 *Grahani*	retention, digestive regulation, controlled progression of food	digestive regulatory complex	not identical to the duodenum or any single organ
2 *Agni*	digestive-metabolic transformative capacity	integrated digestive and metabolic processing	not identical to acid, enzymes, or metabolism alone
3 *Ama*	pathological incompletely transformed state	digestive ecological destabilization / maladaptive substrate state	not identical to toxin or dysbiosis
4 *Samana Vata*	coordination of digestion, retention, and movement	motility and neuroenteric regulatory coordination	not identical to the enteric nervous system
5 *Pittadhara Kala*	digestive interface supporting transformation	mucosal-interface and barrier-regulatory domain	not identical to intestinal mucosa
6 *Basti*	systemic Vata-regulating therapy	distal gut intervention with systems-level therapeutic hypothesis	modern mechanisms remain to be tested

These are conceptual parallels intended for translational dialogue, not direct equivalences.

VII. DIET, MICROBIAL THERAPEUTICS, AND AYURVEDIC PERSONALIZATION

Diet is one of the most immediate points at which classical digestive reasoning and contemporary microbial ecology can be studied together. Food does not act only through nutrient content; it changes luminal water, osmotic load, viscosity, bile acid exposure, fermentation substrate, transit, gas production, and the metabolites available to host tissues. The low-FODMAP diet demonstrates that reducing selected fermentable carbohydrates can improve symptoms in many patients with IBS, but it is not a universal or mechanistically simple treatment. Restriction may reduce distension and fermentation-related symptoms while also changing microbial substrate availability, and prolonged unnecessary restriction can reduce dietary diversity. The relevant lesson for translational Ayurveda is not that one modern diet proves the doctrine of *Agni*. It is that symptom response depends on the interaction among food properties, digestive capacity, timing, dose, transit, and individual susceptibility, which is close to the clinical logic of Matra, Kala, Satmya, Viruddha *Ahara*, and *Pathya-Apathya*. [7,11,30]

An Ayurvedic dietary history can therefore add research value only when it is made reproducible. Broad labels such as heavy, dry, unctuous, incompatible, or *Agni*-weakening should be translated into prespecified observations: meal timing, fasting interval, portion size, cooking method, fat and fiber exposure, dairy and wheat response, spice load, leftovers, ultra-processed foods, alcohol, caffeine, eating speed, emotional context, and symptom latency. The analysis should distinguish immediate intolerance from cumulative effects and should record whether a food changes appetite, postprandial fullness, pain, urgency, stool form, energy, or sleep. This granularity can help test whether Ayurveda-derived patterns identify clinically meaningful dietary phenotypes beyond standard IBS subtype. It also prevents retrospective storytelling in which any food associated

with symptoms is declared incompatible after the outcome is known.

Microbiome-directed therapy remains an instructive example of why ecological plausibility is not sufficient for universal recommendation. Meta-analyses suggest that some probiotics can improve global IBS symptoms or selected outcomes, but heterogeneity in strain, dose, formulation, duration, population, comparator, and risk of bias is substantial. A beneficial result for one strain or combination cannot be generalized to all products bearing the word probiotic. Similarly, fecal microbiota transplantation has produced inconsistent trial results influenced by donor characteristics, route, dose, frequency, placebo design, and patient selection. These findings support microbial involvement in at least some patients while showing that the microbiota is not a single replaceable organ with one ideal composition. [16,31,32]

The same caution applies to sequencing data. Stool samples provide a practical but partial view of the intestinal ecosystem. Taxonomic abundance does not directly establish microbial activity, mucosal location, metabolite flux, or causal relevance. Medication, diet, geography, stool consistency, transit, age, and laboratory pipeline can influence results. Recent meta-analytic work reports recurring microbial differences in IBS, yet substantial between-study variability remains, and no fecal signature is sufficiently validated to diagnose all IBS or all *Grahani* phenotypes. Functional measurements such as short-chain fatty acids, bile acid profiles, fermentation gases, or metagenomic pathways may add information, but even these are context dependent. A metabolite can be beneficial in one concentration and compartment yet associated with symptoms in another. [17,20,21,23]

This uncertainty creates a productive role for Ayurvedic phenotyping. Instead of asking whether *Ama* equals dysbiosis, researchers can ask whether prospectively assessed *Ama*, *Agni*, *Dosha*, appetite, coating, stool characteristics, and postprandial symptom patterns explain part of the biological heterogeneity hidden within the IBS label. The hypothesis would be stronger if Ayurvedic assessment were performed by trained clinicians using a standardized instrument, before microbiome results are available, with inter-rater reliability reported. Investigators could then test whether the categories associate with clinical trajectories, dietary responses, microbial functions, or treatment outcomes. Failure to find such associations would also be informative and should be published. The objective is not to convert classical categories into biomarkers but to determine whether they contribute independent, reproducible stratification.

Personalization must also remain clinically safe. A patient with severe food restriction, weight loss, anemia, nocturnal symptoms, rectal bleeding, persistent fever, family history of colorectal cancer or inflammatory bowel disease, or new symptoms at an older age requires appropriate biomedical evaluation rather than increasingly elaborate dietary classification. Even in confirmed IBS, elimination diets should include nutritional oversight and planned reintroduction. Ayurvedic *Pathya* should support adequate nourishment, cultural feasibility, pleasure, and long-term adherence, not create fear of food. This patient-centered standard is consistent with the classical purpose of restoring strength and digestive stability rather than merely suppressing stool frequency.

A mature integrative model would therefore treat diet as both therapy and experimental probe. A carefully standardized meal challenge could measure symptom timing, motility, stool output, breath gases, selected metabolites, autonomic response, and patient-reported digestive qualities. Repeated within-person observations may be more informative than a single baseline sample because IBS and *Agni* are both variable over time. N-of-1 designs, crossover feeding studies, and adaptive trials could test whether Ayurveda-derived predictions improve selection of diet, probiotic, or digestive intervention. Such designs preserve personalization while producing falsifiable evidence. They also move the field beyond attractive analogies toward a research program in which classical observations must demonstrate added predictive or therapeutic value.

VIII. CRITICAL CORRELATION BETWEEN GRAHANIDOSHA AND IBS

Grahanidosha and IBS are not identical diagnostic entities. IBS is defined through contemporary symptom criteria, bowel subtype, clinical evaluation, and exclusion of selected alternative diagnoses. *Grahanidosha* is diagnosed through a broader Ayurvedic assessment of *Agni*, *Dosha*, *Ama* or *Nirama*

status, stool characteristics, appetite, strength, associated symptoms, and *Samprapti*. A patient who meets modern IBS criteria may not display the same Ayurvedic pattern as another patient with IBS, while some manifestations classified under *Grahanidosha* may correspond to conditions other than IBS and require biomedical investigation.

The most obvious overlap is phenomenological. Both may involve chronic or recurrent abdominal pain or discomfort, bloating, postprandial aggravation, altered stool form, urgency, incomplete evacuation, fluctuating bowel frequency, fatigue, and psychological amplification. Both also allow mixed patterns rather than a single direction of bowel change. Yet similarity of symptoms cannot establish identity because celiac disease, inflammatory bowel disease, microscopic colitis, infection, malabsorption, endocrine disorders, bile acid diarrhea, and other conditions may produce overlapping complaints.

A second overlap lies in functional organization. IBS symptoms may be severe despite the absence of gross structural pathology that fully explains them. *Grahanidosha* similarly emphasizes failure of transformation, retention, and movement rather than a destructive lesion. The comparison is therefore strongest at the level of regulatory instability. It is weaker at the level of molecular mechanism, because classical sources do not describe epithelial tight junctions, microbial genomes, cytokines, neurotransmitters, or central imaging findings.

Direct mapping of IBS subtypes onto *Dosha* categories is particularly unsafe. Loose stool does not by itself establish Pittaja *Grahani*, constipation does not automatically establish *Vata*ja *Grahani*, and mucus or heaviness does not prove Kaphaja *Grahani*. Ayurvedic classification also considers appetite, digestive timing, pain quality, temperature, thirst, strength, tongue, *Ama*, chronicity, diet, and broader constitutional context. Conversely, a *Dosha* diagnosis does not replace modern evaluation for celiac disease, inflammatory bowel disease, microscopic colitis, bile-acid diarrhea, infection, malignancy, thyroid disease, medication effects, or pelvic-floor dysfunction when clinically indicated. The most defensible integration is parallel phenotyping: establish the contemporary diagnosis and exclusions, then independently characterize the Ayurvedic pattern and examine whether that pattern predicts prognosis or treatment response. [5,7]

A third overlap concerns psychophysiological influence. Classical etiological discussions recognize worry, grief, fear, and inappropriate behavior as factors capable of disturbing digestion. Modern IBS research demonstrates that stress and affective processes can alter both symptom perception and gastrointestinal physiology. This convergence supports integrated assessment of mental and digestive factors without reducing either disease model to a purely psychological explanation.

The *Atisara*-to-*Grahani* sequence and post-infectious IBS provide another useful but limited comparison. Both recognize chronic digestive instability following an acute diarrheal event. However, post-infectious IBS has specific epidemiologic and mechanistic definitions, whereas the classical progression is framed through unresolved *Agni* impairment and premature dietary or behavioral exposure. They should be compared as parallel patterns of chronicity, not treated as synonymous diagnoses.

The most defensible conclusion is that *Grahanidosha* is a broader Ayurvedic model of chronic digestive regulatory dysfunction that overlaps with selected clinical and pathophysiological dimensions of IBS. It may assist in generating Ayurvedic phenotypes and individualized treatment hypotheses, but modern diagnosis, red-flag assessment, and appropriate investigation remain necessary. Table 2 summarizes the principal similarities and differences.

Table 2. Grahanidosha And IBS: Similarities And Differences

Domain	Grahanidosha	IBS	Interpretive status
Diagnostic framework	Agni, Dosha, Ama, stool, appetite, strength, and Samprapti	Rome symptom criteria, bowel subtype, and targeted evaluation	Different systems
Core disturbance	Impaired transformation, retention, and movement	Heterogeneous disorder of gut-brain interaction	Partial systems-level overlap
Bowel pattern	Loose, formed,	IBS-D, IBS-C,	Phenomenological overlap;

Domain	Grahanidosha	IBS	Interpretive status
	hard, mixed, or alternating according to stage and Dosha	IBS-M, and IBS-U	no direct mapping
Pain and sensitivity	Pain or discomfort within Dosha- and Agni-specific patterns	Visceral hypersensitivity and altered pain processing in subsets	Possible clinical overlap
Psychological influence	Worry, grief, fear, and behavior may disturb digestion	Stress, anxiety, mood, hypervigilance, and central processing influence symptoms	Strong conceptual overlap; different terminology
Post-infective pattern	Chronic Grahani disturbance may follow unresolved Atisara	Post-infectious IBS after acute enteritis	Parallel pattern, not equivalence
Therapeutic framework	Agni correction, Ama management, diet, behavior, and Dosha-specific therapy	Dietary, behavioral, pharmacologic, and phenotype-directed management	Complementary research domains

IX. A FIVE-LAYER TRANSLATIONAL MODEL: FROM AGNI IMPAIRMENT TO MICROBIOTA-GUT-BRAIN DYSREGULATION

A useful synthesis can be constructed through five interacting layers without collapsing either system into the other. The first is the transformative layer, represented in Ayurveda by *Agni* and supported by *Pachaka Pitta*. Its biomedical comparison domain includes digestive secretion, enzymatic processing, bile-mediated transformation, absorptive preparation, metabolic signaling, and the timing required for these processes. The correspondence is functional, not material: *Agni* is not an enzyme, acid, hormone, or caloric measurement. The research question generated by this layer is whether defined Ayurvedic patterns of impaired transformation correspond to reproducible differences in meal response, transit, stool phenotype, metabolite exposure, or symptom timing.

The second is the substrate-ecology layer. *Ama* denotes pathological incompleteness and incompatibility after defective transformation. In a modern digestive ecosystem, incompletely absorbed or differently processed substrates can alter osmotic load, fermentation, gas production, metabolite profiles, and ecological selection pressures. Yet *Ama* cannot be identified with fecal bacteria, endotoxin, small-intestinal bacterial overgrowth, or one metabolomic signature. A testable translation would instead ask whether clinically defined *Ama*-positive and *Nirama* phenotypes differ in diet, stool chemistry, fermentation-related symptoms, microbial function, or response to *Dipana-Pachana* strategies. Such studies require operational Ayurvedic criteria defined before laboratory results are known, preventing biomarkers from being used retrospectively to manufacture equivalence.

The third is the interface layer, represented by *Pittadhara Kala* as a support for digestive transformation. The modern comparison domain includes epithelial barrier regulation, mucus, immune tolerance, enteroendocrine signaling, host-microbial contact, and sensory communication. *Pittadhara Kala* is not the histological mucosa, but the comparison directs attention to the condition of the digestive boundary across which transformation becomes host physiology. The fourth is the movement-regulation layer, represented by *Samana Vata* and *Apana Vata*. It includes retention, mixing, propulsion, separation, and evacuation, with modern comparison domains in motility, enteric reflexes, autonomic regulation, pelvic-floor coordination, and transit. Neither layer is reducible to one tissue or nervous pathway. [12,18,19]

The fifth is the central-affective layer. Classical etiological descriptions acknowledge worry, fear, grief, irregular behavior, and other disturbances that can weaken digestion or aggravate established disease. Contemporary models describe bidirectional signaling among central networks, autonomic pathways, the

hypothalamic-pituitary-adrenal axis, immune mediators, visceral afferents, and microbial metabolites. Psychological factors are neither imaginary causes nor mere consequences: they can influence attention, threat appraisal, motility, permeability, immune activity, pain amplification, and treatment behavior. In turn, unpredictable bowel symptoms can increase hypervigilance, avoidance, shame, and anxiety. This recursive structure explains why brain-gut behavioral therapies can improve abdominal pain in selected patients without implying that the disease is purely psychological. [27-29]

The five layers form a bidirectional network rather than a linear historical translation. Impaired transformation may alter the substrate environment; substrate changes may influence microbiota and the interface; interface signaling may amplify sensation and motility; stress may worsen movement and barrier regulation; and unstable transit may further change substrate delivery and microbial activity. The model predicts that successful treatment need not normalize every layer simultaneously and that different patients may enter the cycle at different points. It also explains why a single stool microbiome sample, serum marker, or symptom score cannot represent the whole disorder. The value of the framework is its capacity to organize multidomain measurement while preserving a central Ayurvedic insight: durable digestive health depends on coordinated transformation, containment, movement, and adaptation.

Table 3. Five-Layer Translational Model And Research Boundaries

Layer	Ayurvedic organization	Modern comparison domain	Research boundary
Transformation	Agni and Pachaka Pitta	Digestion, secretion, absorptive preparation, metabolic signaling	Test meal response, transit, symptoms, and metabolite exposure; no one-to-one identity
Substrate ecology	Ama and incomplete transformation	Osmotic load, fermentation, luminal chemistry, microbial substrate availability	Compare prospectively defined Ama/Nira ma phenotypes; Ama is not dysbiosis
Digestive interface	Pittadhara Kala	Barrier, mucus, immune tolerance, enteroendocrine and host-microbial signaling	Measure selected interface markers; Pittadhara Kala is not mucosa
Movement-regulation	Samana Vata and Apana Vata	Motility, transit, enteric-autonomic and evacuation coordination	Use validated transit and bowel outcomes; Vata is not the nervous system
Central-affective regulation	Psychological and behavioral etiologies	Central processing, stress physiology, autonomic and behavioral feedback	Use validated measures without psychologizing symptoms

X. PRIYANGVADI BASTI: CLASSICAL RATIONALE AND RESEARCH HYPOTHESIS

The therapeutic management of *Grahanidosha* follows *Samprapti-vighatana*, the interruption of the pathogenic sequence. Early or *Ama*-dominant stages require attention to *Agni*, digestion, diet, and the processing of pathological incompleteness. Chronic disease may additionally involve *Vata*-mediated instability of retention, transit, and evacuation. In such contexts, treatment is not directed solely at reducing stool frequency; it aims to restore organized digestive function while preserving the patient's strength.

Basti is regarded in classical Ayurveda as a principal intervention for *Vata* disorders. Its relevance to *Grahanidosha* arises from the role of *Samana Vata* and *Apana Vata* in digestive coordination and

elimination. A rectal route does not automatically imply a purely local laxative action within Ayurvedic therapeutics. Depending on composition and clinical indication, *Basti* may be evacuative, nourishing, stabilizing, or specifically *Grahi*. Charaka emphasizes the systemic therapeutic importance of *Basti* in *Vata*-predominant disease. [34]

Grahi is often translated as antidiarrheal, but this is incomplete. The term conveys the capacity to support appropriate retention and reduce pathological looseness after adequate digestion. A *Grahi* intervention is therefore most appropriate when excessive mobility or poor containment persists in a context where obstructive *Ama* has been addressed or carefully assessed. Suppressing diarrhea indiscriminately in an *Ama*-dominant or infectious condition would not follow this therapeutic logic.

The *Sushruta Samhita* describes *Grahi Basti* in the management of chronic bowel instability and includes Priyangu among relevant ingredients in formulations intended to promote retention. [35] The designation *Priyangvadi Basti* in the present review refers to a formulation developed from this *Grahi* therapeutic rationale. Before publication, the exact classical source, ingredient identity, botanical authentication, quantity, preparation method, sequence, dose, accompanying Anuvasana or Niruha schedule, and indication must be documented from the protocol actually used. The current literature does not justify treating every similarly named formulation as identical.

The textual formulation deserves precise reporting because the name Priyangvadi can refer to different preparations across contexts. In the Sushruta passage relevant to *Grahi Basti*, a decoction of the Priyangvadi group is combined with a paste of the Ambasthadi group and suitable adjuncts; the following verse also describes medicated oil or ghee prepared with related drugs for Sneha *Basti*. The therapeutic identity therefore depends on the exact source, ingredient list, botanical species, plant part, pharmaceutical process, dose, and whether the intervention is Niruha, Anuvasana, or a protocol combining both. A publishable study must distinguish the classical textual formulation from any investigator-adapted version and provide quality-control information sufficient for replication. [35]

The modern mechanism of *Priyangvadi Basti* is unknown. Several research domains are plausible but must remain explicitly hypothetical. Changes in stool frequency and consistency may reflect altered distal colonic transit, fluid handling, or evacuation dynamics. Rectal administration may interact with mucosal, neural, immune, and microbial environments, but direct systemic effects cannot be inferred from route alone. Any claim concerning cytokines, serotonin, vagal tone, tight-junction proteins, microbial diversity, or specific metabolites requires direct measurement and an appropriate control group.

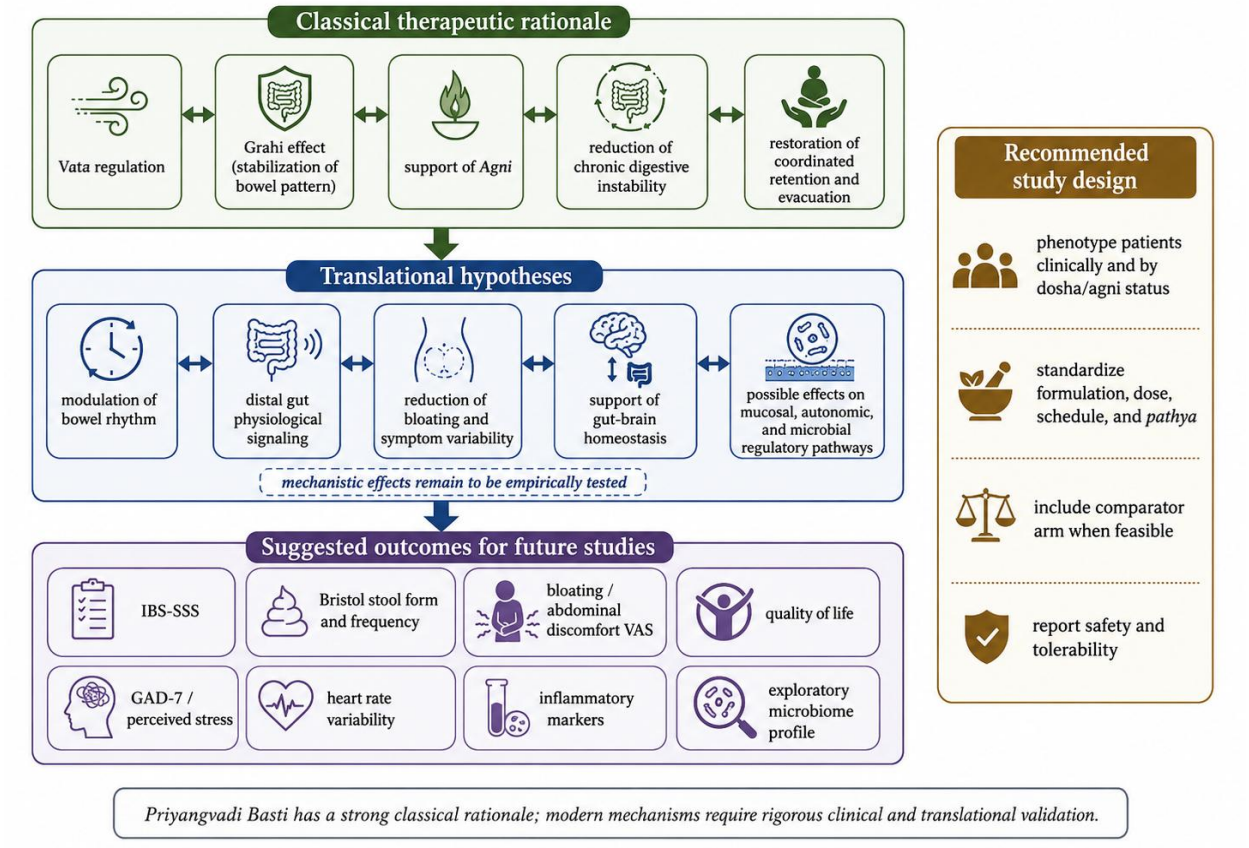
The most immediate translational hypothesis concerns bowel-pattern stabilization. A therapy selected for *Vata*-mediated irregularity and defective retention should first be evaluated through validated clinical endpoints: pain, bloating, urgency, stool form, stool frequency, incomplete evacuation, adequate relief, quality of life, and durability of response. Mechanistic sampling should be secondary and prespecified. Exploratory findings from small, uncontrolled studies should not be presented as proof that the intervention restores the microbiome or gut-brain axis.

Priyangvadi Basti should also be understood as one component of a broader treatment package rather than an isolated pharmacological exposure. Ayurvedic management may include preparatory measures, diet, timing of meals, oral *Dipana-Pachana* or *Grahi* medicines, rest, behavioral advice, and follow-up *Pathya*. These co-interventions can influence outcomes and must be standardized or reported transparently. Otherwise, the specific contribution of the *Basti* cannot be distinguished from the effect of the whole therapeutic program.

Mechanistic research should also respect the intervention's procedural nature. Rectal administration involves solution composition, osmolarity, viscosity, temperature, volume, administration speed, retention time, posture, bowel preparation, concurrent oil-based *Basti*, and practitioner technique. Each factor can influence tolerability, evacuation, fluid movement, and local exposure. A pharmacological description of ingredients alone is therefore insufficient. Likewise, sham control is difficult because volume, sensation, and evacuation can reveal allocation. Early studies may be better framed as assessor-blinded, controlled pragmatic trials with transparent co-intervention reporting, followed by mechanistic substudies once a clinically credible signal and safe protocol are established.

Accordingly, the scientific importance of *Priyangvadi Basti* lies not in a presumed ancient description of modern molecular pathways, but in a coherent classical indication that can be tested rigorously. The priority is to establish safety, feasibility, clinical effect, phenotype-specific response, and treatment durability before advancing to costly multi-omic or neuroimmune studies.

Figure 3. Priyangvadi Basti: classical rationale and future research framework



XI. FUTURE RESEARCH DIRECTIONS

Future studies should recruit patients using clearly stated contemporary diagnostic criteria and report whether Rome IV or Rome V clinical or research criteria were applied. IBS-D, IBS-C, IBS-M, and post-infectious phenotypes should not be pooled automatically. Ayurvedic phenotyping should be recorded prospectively, including *Agni* pattern, *Ama* or *Nirama* status, dominant *Dosha*, stool characteristics, appetite, strength, and relevant dietary or psychological factors. This would permit analysis of whether specific Ayurvedic patterns predict response rather than assuming a uniform *Grahani*-IBS correspondence.

A controlled feasibility study should standardize the *Priyangvadi Basti* formulation, botanical identity, preparation, dose, schedule, route, retention time, accompanying therapies, *Pathya*, rescue medication, and follow-up. Safety monitoring should include adverse events, worsening pain, bleeding, dehydration, electrolyte disturbance where clinically relevant, and discontinuation criteria. The comparator may be usual care, a matched Ayurveda program without *Basti*, or another ethically justified control depending on the research question.

Validated outcomes should be prespecified. The IBS Symptom Severity Scoring System can quantify global severity, the Bristol Stool Form Scale can describe stool consistency, and the IBS-specific quality-of-life instrument can assess broader disease impact. [36-38] Daily stool frequency, urgency, incomplete evacuation, pain, bloating, patient global improvement, medication use, and recurrence after

treatment are also clinically meaningful. Mechanistic endpoints should be limited to a small feasible set, such as heart-rate variability, selected inflammatory or permeability markers, stool microbiome or metabolite profiling, rather than an unfocused panel vulnerable to false-positive findings.

To improve reproducibility, investigators should publish a treatment manual and a core dataset. The manual should define patient preparation, decision rules for postponing or stopping *Basti*, formulation testing, administration competency, permitted oral medicines, dietary instructions, and management of adverse events. The core dataset should include the modern diagnosis, bowel subtype, symptom duration, post-infective status, major exclusions, medication exposure, menstrual or hormonal context where relevant, diet, antibiotic and probiotic use, and prespecified Ayurvedic variables. Microbiome studies should record collection time, storage, extraction, sequencing, bioinformatic pipeline, and multiple-testing correction. These details are less glamorous than molecular claims, but they determine whether another group can reproduce or refute the findings.

Table 4. Proposed Research Outcomes For Priyangvadi Basti

Research domain	Suggested outcome	Rationale
Clinical severity	IBS Symptom Severity Scoring System	Captures pain, bloating, bowel dissatisfaction, and life interference
Stool pattern	Bristol Stool Form Scale and daily frequency	Documents consistency and bowel rhythm
Pain and bloating	Validated numerical or visual analog scales	Measures dominant symptom burden
Urgency/evacuation	Daily diary and incomplete-evacuation rating	Assesses functional bowel control
Psychological status	Validated anxiety and perceived-stress measures	Examines psychodigestive association
Autonomic regulation	Heart-rate variability with standardized acquisition	Exploratory assessment of autonomic balance
Quality of life	IBS-specific quality-of-life instrument	Measures patient-centered impact
Exploratory biology	Prespecified microbiome, metabolite, inflammatory, or permeability measures	Tests mechanism without overinterpreting clinical response

XII. LIMITATIONS

This is a narrative translational review rather than a systematic review, and selection and interpretation of sources may therefore be influenced by author judgment. Ayurvedic and biomedical concepts arise from different observational, diagnostic, and evidentiary traditions; every comparison is partial. Classical terminology has been rendered without diacritics to follow the target journal's formatting instructions, reducing philological precision. Exact page numbers, editions, and commentarial readings of several classical passages require final verification from the author's physical texts.

IBS is heterogeneous, and findings concerning microbiota, permeability, immune activation, visceral hypersensitivity, autonomic regulation, or psychological factors do not apply uniformly to every patient. Group-level associations do not establish causation or provide an individual biomarker. Direct controlled evidence for *Priyangvadi Basti* in patients defined by contemporary IBS criteria is limited. Therefore, proposed relationships with transit, microbiota, epithelial barrier function, inflammatory

signaling, autonomic balance, or gut-brain communication remain research hypotheses rather than demonstrated mechanisms. The manuscript also does not assess the comparative safety or effectiveness of this intervention against established IBS treatments.

XIII. CONCLUSION

Grahanidosha is a classical Ayurvedic model of chronic digestive dysregulation in which impaired *Agni*, incomplete transformation, disturbed retention, *Vata*-mediated instability, and altered digestive interface function interact. IBS is a contemporary disorder of gut-brain interaction characterized by pain or discomfort and altered bowel habits, with variable contributions from motility, visceral sensitivity, microbiota, barrier physiology, immune activity, autonomic regulation, prior infection, and psychosocial factors.

The two conditions should not be declared identical. Their most meaningful convergence lies at the level of regulatory architecture: both recognize that persistent symptoms can arise from unstable coordination rather than a single gross lesion. *Ama* is not dysbiosis, *Pittadhara Kala* is not intestinal mucosa, and *Vata* is not the nervous system. These boundaries do not diminish the value of comparison; they make the resulting hypotheses more precise and testable.

Priyangvadi Basti has a coherent classical rationale as a *Grahi* and *Vata*-regulating intervention, but its efficacy, safety, phenotype specificity, and biomedical mechanisms require direct investigation. A rigorous research program should combine verified textual scholarship, standardized formulations and procedures, contemporary diagnostic criteria, validated patient-centered outcomes, appropriate controls, adequate follow-up, and a limited number of prespecified mechanistic measures.

For this field to mature, future publications should make disagreement visible rather than smoothing it away. Negative trials, phenotype-specific responses, protocol deviations, adverse events, and unchanged biomarkers are scientifically informative. Classical reasoning should be documented prospectively before outcomes are known, while laboratory interpretation should be blinded to Ayurvedic categories whenever feasible. Multicenter replication should precede claims of diagnostic biomarkers, universal mechanisms, or broad therapeutic superiority. Patient priorities should guide outcome selection because a statistically detectable microbial shift may be clinically irrelevant, whereas reduced urgency, restored confidence in eating, improved sleep, and sustained participation in daily life may be deeply meaningful. Transparent registration, open analytical code, deposited sequencing data, authenticated medicines, and independent safety monitoring would allow the proposed framework to be challenged constructively. Future scholarship must also distinguish conceptual usefulness from therapeutic effectiveness: a framework may organize observations elegantly yet fail to predict outcomes, and an intervention may improve symptoms without confirming its proposed mechanism. Respect for Ayurveda requires neither exaggeration nor defensive equivalence. It requires disciplined textual interpretation, clinically meaningful questions, reproducible methods, publication of null findings, and willingness to revise hypotheses when evidence does not support them. This scientific humility offers the strongest foundation for credible, ethical, and internationally relevant integrative gastroenterology research and defensible clinical application across diverse populations worldwide.

XIV. LIST OF ABBREVIATIONS

DGBI - disorder of gut-brain interaction
ENS - enteric nervous system
FODMAP - fermentable oligosaccharides, disaccharides, monosaccharides, and polyols
GI - gastrointestinal
HPA - hypothalamic-pituitary-adrenal
HRV - heart-rate variability
IBS - irritable bowel syndrome
IBS-C - constipation-predominant IBS
IBS-D - diarrhea-predominant IBS
IBS-M - mixed-bowel-pattern IBS
IBS-SSS - Irritable Bowel Syndrome Symptom Severity Score
SCFA - short-chain fatty acid
VAS - visual analog scale

REFERENCES

[1] Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. Lancet. 2020;396(10263):1675-1688.

doi:10.1016/S0140-6736(20)31548-8. Available from: https://doi.org/10.1016/S0140-6736(20)31548-8

[2] Drossman DA, Chang L, Tack J. Disorders of gut-brain interaction and the Rome V process. Gastroenterology. 2026;170(6):1083-1098. doi: 10.1053/j.gastro.2026.02.014. Available from: https://doi.org/10.1053/j.gastro.2026.02.014

[3] Drossman DA, Hasler WL. Rome IV-functional gastrointestinal disorders: disorders of gut-brain interaction. Gastroenterology. 2016;150(6):1257-1261. doi: 10.1053/j.gastro.2016.03.035. Available from: https://doi.org/10.1053/j.gastro.2016.03.035

[4] Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. JAMA. 2015;313(9):949-958. doi:10.1001/jama.2015.0954. Available from: https://doi.org/10.1001/jama.2015.0954

[5] Lacy BE, Pimentel M, Brenner DM, Chey WD, Keefer LA, Long MD, et al. ACG clinical guideline: management of irritable bowel syndrome. American Journal of Gastroenterology. 2021;116(1):17-44. doi:10.14309/ajg.0000000000001036. Available from: https://doi.org/10.14309/ajg.0000000000001036

[6] Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, et al. Worldwide prevalence and burden of functional gastrointestinal disorders: results of Rome Foundation Global Study. Gastroenterology. 2021;160(1):99-114.e3. doi: 10.1053/j.gastro.2020.04.014. Available from: https://doi.org/10.1053/j.gastro.2020.04.014

[7] Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut. 2021;70(7):1214-1240. doi:10.1136/gutjnl-2021-324598. Available from: https://doi.org/10.1136/gutjnl-2021-324598

[8] Black CJ, Drossman DA, Talley NJ, Ruddy J, Ford AC. Functional gastrointestinal disorders: advances in understanding and management. Lancet. 2020;396(10263):1664-1674. doi:10.1016/S0140-6736(20)32115-2. Available from: https://doi.org/10.1016/S0140-6736(20)32115-2

[9] Enck P, Aziz Q, Barbara G, Farmer AD, Fukudo S, Mayer EA, et al. irritable bowel syndrome. Nature Reviews Disease Primers. 2016; 2:16014. doi:10.1038/nrdp.2016.14. Available from: https://doi.org/10.1038/nrdp.2016.14

[10] Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features, and Rome IV. Gastroenterology. 2016;150(6):1262-1279.e2. doi:10.1053/j.gastro.2016.02.032. Available from: https://doi.org/10.1053/j.gastro.2016.02.032

[11] Tripathi B, editor. Charaka Samhita of Agnivesha, Chikitsasthana, Grahani Dosha Chikitsa, chapter 15, verses 51-57. Revised edition. Varanasi: Chaukhamba Surbharati Prakashan; 2002. [Edition, page, and verse wording must be verified against the author's cited copy.]

[12] Shastri AD, editor. Sushruta Samhita of Sushruta, Sharirasthana, Garbha Vyakarana Sharira, chapter 4, verses 18-19. Varanasi: Chaukhamba Sanskrit Sansthan; 2012. p.40. [Verify against the author's cited copy.]

[13] Murthy KRS, editor and translator. Ashtanga Hridaya of Vagbhata, Nidanasthana, Atisara-Grahani Dosha Nidana, chapter 8. Varanasi: Chowkhamba Krishnadas Academy; edition and page to be verified by the author.

[14] Klem F, Wadhwa A, Prokop LJ, Sundt WJ, Farrugia G, Camilleri M, et al. Prevalence, risk factors, and outcomes of irritable bowel syndrome after infectious enteritis: a systematic review and meta-analysis. Gastroenterology. 2017;152(5):1042-1054.e1. doi: 10.1053/j.gastro.2016.12.039. Available from: https://doi.org/10.1053/j.gastro.2016.12.039

[15] Barbara G, Grover M, Bercik P, Corsetti M, Ghoshal UC, Ohman L, et al. Rome Foundation Working Team report on post-infection irritable bowel syndrome. Gastroenterology. 2019;156(1):46-58.e7. doi: 10.1053/j.gastro.2018.07.011. Available from: https://doi.org/10.1053/j.gastro.2018.07.011

[16] Kraimi N, Ross T, Pujo J, De Palma G. The gut microbiome in disorders of gut-brain interaction. Gut Microbes. 2024;16(1):2360233. doi:10.1080/19490976.2024.2360233. Available

from: https://doi.org/10.1080/19490976.2024.2360233

[17] Ju X, Jiang Z, Ma J, Yang D. Changes in fecal short-chain fatty acids in IBS patients and effects of different interventions: a systematic review and meta-analysis. Nutrients. 2024;16(11):1727. doi:10.3390/nu16111727. Available from: https://doi.org/10.3390/nu16111727

[18] Holtmann GJ, Ford AC, Talley NJ. Pathophysiology of irritable bowel syndrome. Lancet Gastroenterology & Hepatology. 2016;1(2):133-146. doi:10.1016/S2468-1253(16)30023-1. Available from: https://doi.org/10.1016/S2468-1253(16)30023-1

[19] Mayer EA, Tillisch K, Gupta A. Gut/brain axis and the microbiota. Journal of Clinical Investigation. 2015;125(3):926-938. doi:10.1172/JCI76304. Available from: https://doi.org/10.1172/JCI76304

[20] Pittayanon R, Lau JT, Yuan Y, Leontiadis GI, Tse F, Surette M, et al. Gut microbiota in patients with irritable bowel syndrome: a systematic review. Gastroenterology. 2019;157(1):97-108. doi: 10.1053/j.gastro.2019.03.049. Available from: https://doi.org/10.1053/j.gastro.2019.03.049

[21] Li X, Li X, Xiao H, Xu J, He J, Xiao C, et al. Meta-analysis of gut microbiota alterations in patients with irritable bowel syndrome. Frontiers in Microbiology. 2024; 15:1492349. doi:10.3389/fmicb.2024.1492349. Available from: https://doi.org/10.3389/fmicb.2024.1492349

[22] Cryan JF, O'Riordan KJ, Cowan CSM, Sandhu KV, Bastiaanssen TFS, Boehme M, et al. The microbiota-gut-brain axis. Physiological Reviews. 2019;99(4):1877-2013. doi:10.1152/physrev.00018.2018. Available from: https://doi.org/10.1152/physrev.00018.2018

[23] Luo M, Zhuang X, Tian Z, Xiong L. Alterations in short-chain fatty acids and serotonin in irritable bowel syndrome: a systematic review and meta-analysis. BMC Gastroenterology. 2021; 21:14. doi:10.1186/s12876-020-01577-5. Available from: https://doi.org/10.1186/s12876-020-01577-5

[24] Hanning N, Edwinson AL, Ceuleers H, Peters SA, De Man JG, Hassett LC, et al. Intestinal barrier dysfunction in irritable bowel syndrome: a systematic review. Therapeutic Advances in Gastroenterology. 2021; 14:1756284821993586. doi:10.1177/1756284821993586. Available from: https://doi.org/10.1177/1756284821993586

[25] Camilleri M. Leaky gut: mechanisms, measurement and clinical implications in humans. Gut. 2019;68(8):1516-1526. doi:10.1136/gutjnl-2019-318427. Available from: https://doi.org/10.1136/gutjnl-2019-318427

[26] Barbara G, Stanghellini V, De Giorgio R, Cremon C, Cottrell GS, Santini D, et al. Activated mast cells in proximity to colonic nerves correlate with abdominal pain in irritable bowel syndrome. Gastroenterology. 2004;126(3):693-702. doi: 10.1053/j.gastro.2003.11.055. Available from: https://doi.org/10.1053/j.gastro.2003.11.055

[27] Qin HY, Cheng CW, Tang XD, Bian ZX. Impact of psychological stress on irritable bowel syndrome. World Journal of Gastroenterology. 2014;20(39):14126-14131. doi:10.3748/wjg.v20.i39.14126. Available from: https://doi.org/10.3748/wjg.v20.i39.14126

[28] Liu Q, Wang EM, Yan XJ, Chen SL. Autonomic functioning in irritable bowel syndrome measured by heart rate variability: a meta-analysis. Journal of Digestive Diseases. 2013;14(12):638-646. doi:10.1111/1751-2980.12092. Available from: https://doi.org/10.1111/1751-2980.12092

[29] Goodoory VC, Khasawneh M, Thakur ER, Everitt HA, Gudleski GD, Lackner JM, et al. Effect of brain-gut behavioral treatments on abdominal pain in irritable bowel syndrome: systematic review and network meta-analysis. Gastroenterology. 2024;167(5):934-943.e5. doi: 10.1053/j.gastro.2024.05.010. Available from: https://doi.org/10.1053/j.gastro.2024.05.010

[30] Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. Gastroenterology. 2014;146(1):67-75.e5. doi: 10.1053/j.gastro.2013.09.046. Available from: https://doi.org/10.1053/j.gastro.2013.09.046

[31] Goodoory VC, Khasawneh M, Black CJ, Quigley EMM, Moayyedi P, Ford AC. Efficacy of probiotics in irritable bowel syndrome: systematic review and meta-analysis. Gastroenterology. 2023;165(5):1206-1218. doi:

10.1053/j.gastro.2023.07.018. Available from: https://doi.org/10.1053/j.gastro.2023.07.018

[32] Wang Y, Hu Y, Shi P. A meta-analysis of randomized controlled trials evaluating the effectiveness of fecal microbiota transplantation for patients with irritable bowel syndrome. BMC Gastroenterology. 2024; 24:217. doi:10.1186/s12876-024-03311-x. Available from: https://doi.org/10.1186/s12876-024-03311-x

[33] De Palma G, Lynch MDJ, Lu J, Dang VT, Deng Y, Jury J, et al. Transplantation of fecal microbiota from patients with irritable bowel syndrome alters gut function and behavior in recipient mice. Science Translational Medicine. 2017;9(379): eaaf6397. doi:10.1126/scitranslmed. aaf6397. Available from: https://doi.org/10.1126/scitranslmed.aaf6397

[34] Tripathi B, editor. Charaka Samhita of Agnivesha, Siddhisthana, Kalpana Siddhi, chapter 1, verse 40. Varanasi: Chaukhamba Surbharati Prakashan; edition and page to be verified by the author.

[35] Shastri AD, editor. Sushruta Samhita of Sushruta, Chikitsasthana, Niruha Krama Chikitsa, chapter 38, verses 86-88. Varanasi: Chaukhamba Sanskrit Sansthan; edition and page to be verified by the author.

[36] Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Alimentary Pharmacology & Therapeutics. 1997;11(2):395-402. doi:10.1046/j.1365-2036.1997.142318000. x. Available from: https://doi.org/10.1046/j.1365-2036.1997.142318000.x

[37] Lewis SJ, Heaton KW. Stool form scale as a useful guide to intestinal transit time. Scandinavian Journal of Gastroenterology. 1997;32(9):920-924. doi:10.3109/00365529709011203. Available from: https://doi.org/10.3109/00365529709011203

[38] Patrick DL, Drossman DA, Frederick IO, DiCesare J, Puder KL. Quality of life in persons with irritable bowel syndrome: development and validation of a new measure. Digestive Diseases and Sciences. 1998;43(2):400-411. doi:10.1023/A:1018831127942. Available from: https://doi.org/10.1023/A:1018831127942