

**THE INVISIBLE EMPIRE WITHIN: A REVIEW ON THE ROLE OF PANCHAKARMA IN REBOOTING THE GUT'S MICROBIAL MONARCHS****Dr. Manojna S. Maliye<sup>1\*</sup>, Dr. Madhushree H.S.<sup>2</sup>, Dr. Ganesh Puttur<sup>3</sup>**<sup>1\*</sup>Final Year PG Scholar, Department of PG Studies in Panchakarma, Sri Sri College of Ayurvedic Science & Research, Bengaluru.<sup>2</sup>Professor & HOD, Department of PG Studies in Panchakarma, Sri Sri College of Ayurvedic Science & Research, Bengaluru.<sup>3</sup>Professor, Department of PG Studies in Panchakarma, Sri Sri College of Ayurvedic Science & Research, Bengaluru.**\*Corresponding Author: Dr. Manojna S. Maliye**Final Year PG Scholar, Department of PG Studies in Panchakarma, Sri Sri College of Ayurvedic Science & Research, Bengaluru. DOI: <https://doi.org/10.5281/zenodo.23033512>**How to cite this Article:** Dr. Manojna S. Maliye<sup>1\*</sup>, Dr. Madhushree H.S.<sup>2</sup>, Dr. Ganesh Puttur<sup>3</sup> (2026). The Invisible Empire Within: A Review on The Role of Panchakarma In Rebooting The Gut's Microbial Monarchs. World Journal of Pharmaceutical and Medical Research, 12(10), 63–81.

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**ABSTRACT:**

The human gut microbiome is a complex and dynamic microbial ecosystem that plays a vital role in digestion, metabolism, immune regulation, intestinal barrier integrity and maintenance of systemic health. Alterations in its composition and function, collectively termed as gut dysbiosis, have been implicated in the pathogenesis of numerous gastrointestinal and other systemic disorders. Growing evidence has renewed interest in exploring *Ayurveda* and its potential influence on gut microbial homeostasis. This article aims to critically examine the current understanding of the gut microbiome and correlate contemporary concepts with the *Ayurvedic* principles of *Agni*, *Ama* and *Krimi*. It further discusses the probable role of *Panchakarma* in gut microbiome modulation by integrating classical *Ayurvedic* concepts with available scientific evidence and proposed biological mechanisms. Establishing this conceptual bridge may provide new insights into the scientific basis of *Panchakarma* and encourage future experimental and clinical research on microbiome-based integrative therapeutic approaches.

**KEYWORDS:** Gut microbiome, Gut dysbiosis, *Ama*, *Panchakarma*.**INTRODUCTION**

The gut microbiome refers to the characteristic microbial community (bacteria, archaea, viruses, fungi) that inhabits the human gastrointestinal tract, together with their genes (genomes and metagenomes), gene-products (such as metabolites, proteins and signaling molecules), and the local micro-environmental conditions (including mucosa, secreted mucus, immune factors and host cells) in which they operate. *Microbiota* = the collection of microorganisms present and *Microbiome* = microbiota + their genes + their functional environment and interactions.<sup>[1]</sup>

Total number of gut microbes is estimated to an approximate 38 trillion and total number of human cells, about 30 trillion which makes it a 1: 1 ratio. On an average, a single person carries ~5,000 times more microbes than there are humans on earth.

On the other hand, if we take a genetic census, the total number of human genes is about 20 to 23000 and total number of gut microbial genes is around 2 to 3 million which is 100 times more than human genes. This might be the reason for considering the gut microbial genome as the second human genome and consequently a separate organ. Weight of gut microbiome as a whole would be around 1.5 kg that is comparable to the weight of a human brain. Owing to its staunch significance and progressing role in human physiology and pathology, the Human Microbiome Project which was a 170-million-dollar project, funded by the US National Institute of Health was launched in 2 phases to identify, characterize and sequence human microbiota and analyse their role in health and disease.<sup>[2,3,4,5,6]</sup>

Although the gut microbiome is a relatively recent scientific discovery, *Ayurveda* has long recognized the gastrointestinal tract as the cornerstone of health and

disease. Fundamental concepts such as *Agni*, *Ama*, *Kala*, *Koshta*, *Krimi* etc., collectively describe digestive efficiency, metabolic transformation, host-microbial interactions and intestinal homeostasis closely paralleling contemporary concepts of microbial metabolism, gut dysbiosis, intestinal barrier function and immune regulation. Among the various therapeutic modalities described in *Ayurveda*, *Panchakarma* represents the principal bio-purificatory and restorative approach aimed at eliminating vitiated *Doshas*, enhancing *Agni*, restoring normal gastrointestinal function and maintaining *Dhatu Samyata*. Emerging evidence suggests that *Panchakarma* procedures, particularly *Deepana-Pachana*, *Snehapana*, *Virechana* and *Basti*, may influence the gut microbial ecosystem through multiple mechanisms, including improvement of digestive efficiency, regulation of intestinal transit, modulation of bile acid metabolism, restoration of mucosal barrier integrity, immune regulation and ecological restructuring of the intestinal microbiota. Although direct mechanistic and clinical evidence remains limited, these observations provide a plausible scientific basis for exploring *Panchakarma* as a potential microbiome-modulating intervention and establish a conceptual bridge between classical *Ayurvedic* principles and contemporary microbiome science.

## A CENSUS OF THE GUT ECOSYSTEM

Microbial density increases progressively from the stomach to the large intestine, ranging from approximately  $10^1$ – $10^2$  CFU/mL in the stomach and duodenum,  $10^4$ – $10^8$  CFU/mL in the jejunum and ileum and reaching  $10^{10}$ – $10^{12}$  CFU/mL in the colon, which harbours the highest microbial biomass and diversity within the gastrointestinal tract. The reason for this progressive increase in density may be attributed to the strong digestive enzymes, highly acidic pH and rapid gastric emptying as opposed to the relatively neutral pH, abundant undigested carbohydrates and anaerobic environment in the colon.

Although the gut microbiome comprises a diverse array of microorganisms, including bacteria, viruses, fungi, archaea and protozoa, bacteria constitute the predominant microbial population. Among these, the gut microbial community is primarily dominated by Firmicutes (50-60%), Bacteroidetes (25-30%), Proteobacteria (4-6%), Actinobacteria (2-4%), Verrucomicrobia (0.5 -2%) and other minor phyla (less than 1%). Genera like *Clostridium*, *Lactobacillus*, *Ruminococcus*, *Enterococcus*, *Faecalibacterium*, *Roseburia* etc., come under Firmicutes, others like *Bacteroides*, *Prevotella*, *Parabacteroides*, *Alistipes*, *Barnesiella* come under Bacteroidetes phyla.<sup>[7-11]</sup>

## THE MICROBIAL TIMELINE

Table No.1: The Microbial Timeline.

| Life Stage                                                           | Key Features of Gut Microbiome Development                                                                                                                                                                                                                                                                                                                                                                                                                                |
|----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Foetal Stage</b> <sup>[12-15]</sup>                               | Traditionally considered sterile; recent studies suggest low microbial biomass in the placenta, amniotic fluid and meconium, although the existence of a true prenatal microbiome remains controversial.                                                                                                                                                                                                                                                                  |
| <b>Early Neonatal Stage (Birth)</b> <sup>[16,17,18]</sup>            | <b>Mode of delivery</b> determines initial colonization. <b>Vaginal delivery:</b> maternal <i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Bacteroides</i> , <i>Prevotella</i> cause better immune maturation and gut barrier development. <b>Caesarean delivery:</b> predominance of <i>Staphylococcus</i> , <i>Corynebacterium</i> , <i>Cutibacterium</i> , <i>Enterococcus</i> cause delayed anaerobe colonization and increased risk of immune-mediated disorders. |
| <b>Neonate to Early Infancy (1 Week–6 Months)</b> <sup>[19-23]</sup> | Transition from facultative aerobes to obligate anaerobes. <b>Breastfeeding (HMOs):</b> enriches <i>Bifidobacterium</i> , promoting SCFA production, gut barrier integrity and immune tolerance. <b>Formula feeding:</b> higher microbial diversity but fewer <i>Bifidobacterium</i> and relatively less optimal immune programming.                                                                                                                                      |
| <b>Later Infancy (6–12 Months)</b> <sup>[24,25,26]</sup>             | Complementary feeding increases microbial diversity and metabolic capacity. Shift towards fibre-fermenting bacteria ( <i>Bacteroides</i> , <i>Ruminococcus</i> , <i>Faecalibacterium</i> , <i>Roseburia</i> ) with enhanced SCFA production and intestinal maturation.                                                                                                                                                                                                    |
| <b>Toddler Stage (End of First 1000 Days)</b> <sup>[27]</sup>        | Gut microbiome becomes largely stable, diverse and functionally mature, closely resembling the adult microbiome, with continued refinement throughout childhood.                                                                                                                                                                                                                                                                                                          |

## THE ROLE OF MICROBIAL ARCHITECTS IN SHAPING HUMAN PHYSIOLOGY

Table No.2: The Role of Gut Microbiome in Maintaining Equilibrium of Human Physiology.

| Function                                     | Key Role of the Gut Microbiota                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Digestive Function</b> <sup>[28-31]</sup> | Ferments indigestible carbohydrates (fiber, resistant starch, mucins, HMOs) via <i>Bacteroides</i> , <i>Ruminococcus</i> , <i>Faecalibacterium</i> and <i>Bifidobacterium</i> , producing SCFAs (acetate, propionate, butyrate). SCFAs ( short chain fatty acids) provide energy, strengthen the intestinal barrier, regulate glucose and lipid metabolism, modulate immunity, stimulate GLP-1 and PYY secretion, lower colonic pH, inhibit pathogens, enhance calcium and magnesium absorption and support metabolic homeostasis through microbial cross-feeding. |
| <b>Metabolic Function</b> <sup>[32-35]</sup> | Regulates glucose, lipid, bile acid, amino acid and micronutrient metabolism. SCFAs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

|                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                           | enhance insulin secretion and sensitivity (GLP-1, AMPK). Bacterial bile salt hydrolase (BSH) activity generates secondary bile acids that activate FXR and TGR5, promoting fatty acid oxidation, reducing lipogenesis, improving cholesterol metabolism and increasing energy expenditure. Also synthesizes vitamins (K, B-complex), produces bioactive amino acid metabolites and enhances mineral absorption (Ca, Mg, Fe, Zn).                                                                                                                                                                                                                     |
| <b>Immune Function</b> <sup>[36-40]</sup> | Acts as an immunological organ by interacting with GALT (~70% of immune cells). Strengthens epithelial barrier by enhancing tight junction proteins and mucin production, regulates innate immunity through TLRs and NLRs, suppresses pro-inflammatory cytokines and induces antimicrobial peptides. SCFAs promote Treg differentiation, maintain Treg/Th17 balance, enhance IgA production and prevents autoimmunity. Microbial metabolites (SCFAs, secondary bile acids, indoles) further regulate immunity via HDAC inhibition, AhR activation, inflammasome modulation and macrophage polarization, contributing to systemic immune homeostasis. |

## GUT-ORGAN AXES

**GUT-BRAIN AXIS:** It is a bidirectional network linking the gut and brain through neural, endocrine and immune pathways. Around 70–80% of vagus nerve fibres are afferent, transmitting microbial signals to the brain. The SCFAs and neuroactive molecules (serotonin, GABA, dopamine, acetylcholine) regulate blood–brain barrier integrity, microglial maturation, mood, cognition and the HPA axis. Recent studies proved that germ-free mice exhibit exaggerated stress responses, altered BDNF expression and impaired social behaviour, highlighting the microbiome's role in neurodevelopment.<sup>[41,42,43]</sup>

**GUT-HEART AXIS:** Gut microbes convert dietary choline, L-carnitine and phosphatidylcholine into trimethylamine (TMA), which is converted in the liver to trimethylamine-N-oxide (TMAO). Elevated TMAO promotes atherosclerosis, endothelial dysfunction, platelet hyperreactivity and increases the risk of coronary artery disease, myocardial infarction, stroke, and heart failure.<sup>[44,45,46]</sup>

**GUT-LUNG AXIS:** The gut–lung axis links intestinal and pulmonary immunity through microbial metabolites, immune cell trafficking and cytokines. SCFAs promote regulatory T cells, enhance alveolar macrophage function, suppress excessive inflammation and improve defence against respiratory pathogens, reducing the risk and severity of asthma and COPD.<sup>[47,48,49]</sup>

**GUT-BONE AXIS:** SCFAs enhance intestinal calcium absorption by lowering luminal pH and regulate osteoblast and osteoclast activity via immune pathways, promoting bone formation, reducing resorption and maintaining bone mineral density.<sup>[50,51,52]</sup>

**GUT-MUSCLE AXIS:** Microbial SCFAs improve mitochondrial function and energy metabolism, while microbial amino acid metabolism supports muscle protein synthesis. By reducing systemic inflammation, the gut microbiota preserves muscle mass, strength, exercise performance and metabolic health.<sup>[53,54,55]</sup>

**GUT-REPRODUCTIVE AXIS:** The gut microbiota regulates estrogen homeostasis through the estrobolome in females, influencing fertility and menstrual function,

while in males it modulates testosterone metabolism and supports spermatogenesis. SCFAs further promote immune tolerance and endocrine signalling essential for reproductive health.<sup>[56,57,58]</sup>

**GUT-KIDNEY AXIS:** Gut microbes generate uremic toxins such as indoxyl sulfate, p-cresyl sulphate and TMAO. In chronic kidney disease, impaired clearance leads to toxin accumulation, driving systemic inflammation, oxidative stress, endothelial dysfunction and progression of renal and cardiovascular disease.<sup>[59,60,61]</sup>

**GUT-SKIN AXIS:** SCFAs strengthen the skin barrier, regulate keratinocyte differentiation and suppress inflammation through regulatory T cells. By modulating cytokines, oxidative stress and the HPA axis, the gut microbiota influences sebum production, skin immunity and wound healing. Dysbiosis is associated with acne, atopic dermatitis, psoriasis and rosacea.<sup>[62,63,64]</sup>

Under healthy conditions, the interaction is predominantly mutualistic, with the microbiota aiding digestion, vitamin synthesis, immune regulation and colonization resistance while receiving nutrients and a favourable habitat. Some microbes exist as commensals, benefiting without significantly affecting the host. However, dysbiosis, impaired immunity or antibiotic use may transform commensal organisms into opportunistic pathogens, leading to infection. In contrast, pathogenic microorganisms establish parasitic interactions, producing toxins and inducing inflammation that result in host tissue damage and disease. Thus, maintaining a balanced host–microbiome relationship is essential for health and homeostasis.

## GUT DYSBIOSIS AND ITS CAUSES

Gut dysbiosis refers to a disruption in the composition, diversity and functional activity of the gut microbiota, resulting in the loss of normal host–microbe symbiosis and impaired intestinal homeostasis. Dysbiosis can be triggered by multiple factors, including prolonged broad-spectrum antibiotic use, diets rich in fat, sugar and ultra-processed foods low in dietary fibre, chronic psychological stress, aging, sedentary lifestyle, gastrointestinal infections and environmental exposures

such as pollutants, pesticides and food additives. Additional contributors include mode of delivery, infant feeding practices, sleep and circadian disruption, alcohol consumption, smoking and reduced early-life microbial exposure. Dysbiosis is characterized by loss of microbial diversity, reduced production of beneficial metabolites such as short-chain fatty acids (SCFAs), increased intestinal permeability, endotoxin (lipopolysaccharide) translocation, immune dysregulation and altered neuroendocrine signalling, collectively contributing to local and systemic inflammation and the development of metabolic, immune, neurological and gastrointestinal disorders.<sup>[65-69]</sup>

## DIAGNOSTIC STRATEGIES AND TOOLS

The diagnosis of gut dysbiosis involves a combination of an array of techniques as follows<sup>[70-79]</sup>

**1. Clinical evaluation** includes assessment of gastrointestinal symptoms (bloating, abdominal pain, altered bowel habits, food intolerance, reflux), extraintestinal manifestations (fatigue, skin disorders, allergies, autoimmune diseases, anxiety or depression) and risk factors such as recent antibiotic use, chronic stress, poor dietary habits, long-term medications and sedentary lifestyle.

**2. Stool analysis** provides information on microbial composition, diversity, abundance and functional activity.

**3. Microbiome sequencing**, including 16S rRNA gene sequencing and shotgun metagenomic sequencing, enables comprehensive taxonomic and functional characterization of the gut microbiota, including microbial diversity indices ( $\alpha$ - and  $\beta$ -diversity), Firmicutes:Bacteroidetes ratio, metabolic pathways, antibiotic resistance genes and toxin-producing organisms.

**4. Stool culture** remains useful for identifying enteric pathogens such as *Salmonella*, *Shigella*, pathogenic *Escherichia coli*, *Proteus* and *Klebsiella*, although its utility is limited because most gut microbes are anaerobic in nature.

**5. Functional assessment of the microbiome** can be achieved through microbial metabolite analysis, including short-chain fatty acids (SCFAs), branched-chain fatty acids, organic acids, bile acids and tryptophan metabolites using chromatographic and mass spectrometric techniques.

**6. In addition, hydrogen, methane and hydrogen sulfide breath tests** are valuable non-invasive tools for diagnosing small intestinal bacterial overgrowth (SIBO) and carbohydrate malabsorption.

**7. Intestinal permeability** can be assessed using the **lactulose-mannitol test**, where increased lactulose absorption relative to mannitol indicates impaired

epithelial barrier function, while elevated zonulin levels suggest disruption of tight junction integrity.

**8. Additional markers include** lipopolysaccharide (LPS) and intestinal fatty acid-binding protein (I-FABP). Inflammatory biomarkers, including **fecal calprotectin, fecal lactoferrin, secretory immunoglobulin A (sIgA), C-reactive protein (CRP)** and circulating cytokines, aid in evaluating intestinal inflammation and mucosal immune activation.

**9. Advanced multi-omics technologies** such as metagenomics, metatranscriptomics, metaproteomics and metabolomics provide comprehensive insights into microbial composition, gene expression, protein profiles and metabolic function.

**10. Colonoscopy** with mucosal biopsy is valuable for identifying structural abnormalities including inflammation, ulcers, bleeding and polyps.

**11. Standardized symptom-based questionnaires**, such as the **Gastrointestinal Symptom Rating Scale (GSRS), IBS Symptom Severity Score (IBS-SSS), and Rome IV criteria**, facilitate clinical assessment, while commercially available microbiome testing platforms provide personalized analyses of microbial composition and functional profiles.

## INTERVENTIONAL STRATEGIES

**1. Probiotics:** Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. The most extensively studied probiotic microorganisms belong to the genera *Lactobacillus*, *Bifidobacterium*, *Streptococcus* and the yeast *Saccharomyces*. Other examples include *L. rhamnosus*, *L. acidophilus*, *L. plantarum*, *L. casei*, *B. longum*, *B. bifidum*, *B. breve*, *B. infantis*, *Streptococcus thermophilus*, *Saccharomyces boulardii*. These probiotic microorganisms are naturally present in fermented foods such as yogurt, kefir, buttermilk, kimchi, tempeh and fermented vegetables, and are increasingly used as therapeutic adjuncts for restoring gut microbial balance. Probiotics restore gut microbial homeostasis through competitive exclusion of pathogens, production of antimicrobial substances, enhancement of intestinal barrier integrity, modulation of innate and adaptive immune responses and generation of beneficial metabolites such as short-chain fatty acids (SCFAs). Clinically, probiotics are beneficial in the prevention and management of antibiotic-associated diarrhea, *Clostridioides difficile* infection, irritable bowel syndrome (IBS), lactose intolerance and selected cases of inflammatory bowel disease (IBD). Their efficacy is strain and disease-specific, with commonly effective doses ranging from  $10^9$ – $10^{11}$  colony-forming units (CFU)/day.<sup>[80-87]</sup>

**2. Prebiotics:** A substrate that is selectively utilized by host microorganisms conferring a health benefit is called

a prebiotic. Common prebiotics include inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS), resistant starch, xylooligosaccharides (XOS), isomaltoligosaccharides (IMO), polydextrose,  $\beta$ -glucans and pectin, which enhance the growth of *Bifidobacterium* and *Lactobacillus* species and increase short-chain fatty acid (SCFA) production. Natural dietary sources include garlic, onion, leeks, asparagus, chicory root, Jerusalem artichoke, bananas, apples, oats, barley, wheat, beans and lentils.<sup>[88-71]</sup>

**3. Postbiotics** are therapeutics comprising inanimate microorganisms and/or their bioactive metabolites (e.g., short-chain fatty acids, peptides, enzymes and cell wall components) and are known to exert anti-inflammatory, immunomodulatory and barrier-protective effects.

**4. Paraprobiotics** are inactivated or heat-killed microorganisms/probiotics that retain immunomodulatory properties.

**5. Psychobiotics**, particularly selected *Lactobacillus* and *Bifidobacterium* strains, modulate the gut-brain axis and have shown potential in improving mood, anxiety and cognitive function.

**6. Dietary interventions**, including high-fiber diets, resistant starch and polyphenol-rich foods like green tea and berries promote beneficial microbial growth and enhance SCFA production.

**7. Additionally, metabiotics** (purified microbial metabolites or bioactive compounds) and microbiota-directed foods (MDFs) represent promising precision nutrition strategies aimed at modulating microbial composition and function to improve host health.<sup>[92-97]</sup>

**8. Fecal microbiota transplantation (FMT)** is the transfer of processed stool from a carefully screened healthy donor into the gastrointestinal tract of a recipient to restore a healthy gut microbial ecosystem. FMT can be administered through the lower gastrointestinal route (colonoscopy or retention enema), upper gastrointestinal

route (nasogastric, nasoduodenal or nasojejunal tube) or oral encapsulated formulations containing freeze-dried microbiota. Colonoscopic delivery remains the most commonly used method because it enables direct instillation into the colon and has demonstrated high clinical efficacy, whereas oral capsules offer a non-invasive alternative with comparable outcomes in selected patients. FMT is currently the standard of care for recurrent or refractory *Clostridioides difficile* infection and is being investigated for inflammatory bowel disease, irritable bowel syndrome, metabolic disorders and other microbiome-associated diseases.<sup>[98-101]</sup>

## 9. DISCUSSION

### GUT MICROBIOME: THROUGH THE LENS OF AYURVEDA

• Although the references of *Krimi* in classical literature is sparse, one of the earliest references can be found in the *Vedic* literature in the *Krimi Sukta* or *Krimi Nashaka Sukta* present in *Atharva Veda* (*Shaunaka Shakha*) recited by *Rishi Kanva* wherein certain terminologies like *Drishta* & *Adrishta*- visible & invisible; *Matruha Matho* – those living or moving inside the body; *Anvantryam*- those present in the intestine; *Antaha ye asmakam tanvam* – inside our bodies and based on their good or detrimental disease causing effects they are divided into *Sunama* and *Durnama*. Hence, these references indicate an ancient understanding of internal microbial life and its relevance to human health.

• Further *Acharya Charaka* considers *Sahaja Krimi* as one of the types of *Krimi* and *Acharya Chakrapani* considers this type of *Krimi* to be *Shareera Sahaja* and *Avaiakarika* i.e., the microorganisms that are physiologically co-existing in the host system without causing any harm. *Acharya Vagbhata* also opines the same and *Acharya Arunadatta* comments quoting “*Saha Shareerena Jaayanta iti Sahajaaha*” hinting these commensals’ ability of maintaining physiological homeostasis in the human host.<sup>[102,103]</sup>

## BRIDGING GUT DYSBIOSIS, LEAKY GUT AND THE CONCEPT OF AMA

**Table No.3: Differences between a normal physiological gut and leaky gut.**<sup>[104-109]</sup>

| NORMAL PHYSIOLOGICAL GUT BARRIER                                                                                                                                                                                                                                                                                  | LEAKY GUT                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>MICROBIAL BARRIER:</b> It contains more of beneficial bacteria in a normal gut barrier along with their metabolites, cell fragments, antigen load, undigested food particles etc., that help in the production of antimicrobial substances and metabolites like butyrate that maintains gut barrier integrity. | <b>MICROBIAL BARRIER:</b> Due to gut dysbiosis, the microbial diversity shifts to the type which encourages the growth of more pathological microbes than beneficial gut bacteria that leads to the production of endotoxins like lipopolysaccharides and inflammatory metabolites that disrupt the epithelial barrier due to less of butyrate producing bacteria (since butyrate is required for tight junction integrity and permeability maintenance). |
| <b>CHEMICAL BARRIER:</b> It contains the following components:<br>Mucous layer - produced by goblet cells, composed primarily of mucin glycoproteins. The colon has two mucus layers: Inner mucus layer (dense and firmly                                                                                         | <b>CHEMICAL BARRIER:</b><br>Mucus layer thinning- goblet cell function decreases and mucin production declines. Mucus layer becomes thinner; bacteria approach epithelial cells more closely. Reduction of antimicrobial peptides- When Paneth cell                                                                                                                                                                                                       |

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>attached, nearly sterile, prevents bacteria from contacting epithelial cells) and Outer mucus layer (looser, colonized by commensal bacteria);</p> <p>Antimicrobial Peptides- produced by Paneth cells that aids in killing pathobionts;</p> <p>Secretory IgA- that neutralizes toxins.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>function is impaired, bacterial growth increases, microbial invasion of mucosa occurs.</p> <p>Decreased secretory IgA- Reduced IgA levels allow microbes to interact directly with epithelial cells, increasing inflammatory signaling.</p>                                                                                                                                                            |
| <p><b>PHYSICAL BARRIER-</b> It contains the following:</p> <p>Intestinal epithelial cells (Enterocytes- most abundant cells which are responsible for nutrient absorption).</p> <p>Goblet cells (produce mucus).</p> <p>Paneth cells (produce antimicrobial peptides).</p> <p>Enteroendocrine cells (release GI hormones such as: serotonin, GLP-1, peptide YY that regulate digestion and gut motility).</p> <p>M cells (specialized epithelial cells- transport antigens to immune cells in Peyer's patches).</p> <p>Tight junctions: Adjacent epithelial cells are connected by specialized protein complexes called tight junctions.</p> <p>Important tight junction proteins include: claudins, occludin, zonula occludens (ZO-1, ZO-2). These proteins regulate the paracellular pathways which are 2 in number viz.,</p> <p>Transcellular pathway -Substances pass through epithelial cells via transporters. Examples: glucose, amino acids, fatty acids.</p> <p>Paracellular pathway- Substances pass between epithelial cells. This pathway is tightly regulated and normally allows only water and small ions.</p> | <p><b>PHYSICAL BARRIER:</b></p> <p>Tight junction disruption: A key regulator of tight junction integrity is a protein named zonulin and when excessive zonulin is released, the tight junction loosens up and permeability increases leading to the contact of endotoxins and metabolites with the epithelium and the lamina propria layer inturn leading to epithelial injury and oxidative stress.</p> |
| <p><b>IMMUNOLOGICAL BARRIER:</b> The intestine contains one of largest components of the immune system in the body known as Gut-associated lymphoid tissue (GALT) that includes: Peyer's patches, isolated lymphoid follicles, lamina propria immune cells (dendritic cells, macrophages, T lymphocytes, B lymphocytes, plasma cells, mast cells) and intraepithelial lymphocytes.</p> <p>Immune cells in the Lamina Propria detect pathogens while maintaining tolerance to ingested food, antigens and commensal bacteria. Intraepithelial lymphocytes are immune cells embedded between epithelial cells that help in the surveillance of epithelial integrity and elimination of infected epithelial cells.</p>                                                                                                                                                                                                                                                                                                                                                                                                           | <p><b>IMMUNOLOGICAL BARRIER:</b> Disruption of the immune barrier leads to trigger of pro inflammatory cytokines that inturn leads to a vicious inflammatory cascade as follows:</p> <p>Inflammation → barrier damage → increased leakage → more inflammation.</p>                                                                                                                                        |

#### UNDERSTANDING THE PHYSIOLOGICAL ROLE OF GUT MICROBIOME IN THE PROCESS OF DIGESTION AND METABOLISM UNDER THE UMBRELLA OF PACHANA PRAKRIYA, AGNI AND AMA: A HYPOTHESIS

The concept of *Ama* can be understood by correlating *Dhatu Poshana Kriya* with the functional role of the gut microbiome. According to *Ayurveda*, the process of tissue nourishment occurs in three sequential stages: *Pachana*, *Paka* and *Parinama*.

*Pachana* corresponds to the initial mechanical digestion occurring in the oral cavity, oesophagus and stomach, where the ingested food is acted upon by the *Bhutagni*. This is followed by *Paka*, which represents enzymatic digestion in the stomach and small intestine, converting complex food into absorbable nutrients which is mainly acted upon by *Jatharagni*. The final stage, *Parinama*,

involves absorption, assimilation and metabolism, during which it is mainly acted upon by the *Dhatwagni* and this is probably the stage where the gut microbiome plays a pivotal role.

The *Sara Bhaga* (nutritive fraction) undergoes further microbial biotransformation, generating metabolites that support tissue nourishment and homeostasis. Simultaneously, the *Kitta Bhaga*, particularly resistant starch and dietary fibre, is fermented by gut microbiota into short-chain fatty acids (SCFAs), especially butyrate, which serves as the primary energy source for nearly 70% of colonocytes and is essential for maintaining intestinal barrier integrity and immune balance. This highlights the physiological significance of *Kitta Bhaga*, providing a probable rationale for the *Ayurvedic* dictum "*Balam Tasya Hi Vidbalam*."

The functions of the gut microbiome also parallel the classical *Dhatu Poshana Nyayas*.

1. *Ksheera-Dadhi Nyaya* is reflected in the sequential microbial transformation of dietary substrates into SCFAs.
2. *Kedara-Kulya Nyaya* corresponds to the tissue-specific actions of microbial metabolites such as indole derivatives and GABA.
3. *Khale-Kapota Nyaya* is exemplified by substrate-specific microbial metabolism, such as the selective

utilization of human milk oligosaccharides by *Bifidobacterium* species.

Thus, the gut microbiome may be considered an important functional manifestation (*Avayava*) of *Agni*, contributing to digestion, metabolism, tissue nourishment, and maintenance of physiological homeostasis. Conversely, gut dysbiosis may impair these functions, resulting in incomplete digestion and metabolism, thereby contributing to the formation of *Ama*.

**Table No.4: Bridging Gut Dysbiosis, Leaky Gut and the Concept of Ama.**

| ASPECT             | CONCEPT OF LEAKY GUT                                                                 | CONCEPT OF AMA                                                                                                         | PARALLEL                                                    |
|--------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|
| CORE CONCEPT       | Increased intestinal permeability allowing toxins to enter circulation               | धातुमाद्यमपाचितम्<br>दुष्टमामाशयगतं रसमामं प्रचक्षते<br>(Toxic metabolic by-products formed due to impaired digestion) | Both involve toxic substances entering systemic circulation |
| ORIGIN             | Dysfunction of intestinal barrier, gut dysbiosis                                     | ऊष्मणोऽल्पबलत्वेन- Impaired <i>Agni</i> (digestive/metabolic fire)                                                     | Both start with digestive dysfunction                       |
| NATURE OF TOXIN    | LPS, endotoxins, microbial metabolites                                               | अविपक्वमसंयुक्तं दुर्गन्धं बहु पिच्छिलम्- sticky, toxic, undigested metabolic residue                                  | Both represent harmful metabolic toxins                     |
| SITE OF FORMATION  | Gut lumen (especially colon)                                                         | <i>Amashaya (Annavaaha srotas)</i>                                                                                     | The Gastrointestinal tract                                  |
| SYSTEMIC EFFECTS   | Metabolic endotoxemia → systemic inflammation, insulin resistance, neuroinflammation | Low-grade inflammation ( <i>Amajanya Jwara</i> )                                                                       | Both showcase systemic effects                              |
| Effect on Channels | Causes <i>Srotorodha</i>                                                             | Damages microcirculation + immune activation                                                                           | Causes damage to both micro and systemic circulation        |

#### PROBABLE ROLE OF PACHANA DEEPANA IN GUT MICROBIOME RESTORATION

**1. Stimulation of Digestive Secretions → Reduced Dysbiotic Substrate Load:** *Pachana Deepana Dravyas* contain certain active principles like gingerol, piperine, thymols, picrosides that help in increasing gastric acid and digestive enzyme secretion that in turn helps in complete or partial digestion of most of the dysbiotic bacterial substrates before reaching the colon that leaves no or less substrate for the pathobionts to feed on, hence correcting dysbiosis. This might also be the reason why *Pachana Deepana* is continued till *Ama Nirharana* is attained and *Srotorodha* is eliminated.

**2. Bioactive phytochemicals directly influence microbial growth-** These phytochemicals present in *Pachana Deepana Dravyas* are also known to have certain selective antimicrobial properties wherein they disrupt bacterial cell membranes, interfere with microbial enzyme systems, alter bacterial quorum sensing signals and prevent pathogenic biofilm formation favoring a commensal eubiotic environment.

**3. Improved Gastrointestinal Motility → Prevention Of Microbial Stasis-** *Pachana Deepana* drugs are also said to increase gut motility by secretion of bile acids and motilin hormone that prevents stasis of intestinal contents leading to dynamic evacuation of bad bacteria and their metabolites in the further processes. Therefore, *Anila Moodhata* which is one of the *Sama Lakshanas* is reduced after giving *Pachana Deepana* that leads to *Vatanulomana*.

**4. Prebiotic Potential of Several Pachana Deepana Herbs-** Many *Pachana Deepana Dravyas* contain polyphenols in them that act as substrate and stimulate the growth of good bacteria like lactobacilli and bifidobacterium and also help in anti-inflammatory action. Eg: Ginger contains polysaccharides, cumin contains hemicellulose etc. Along with this during *Ruksha Purva Snehapana*, in cases of *Sthoulya* etc., *Takra* is given for internal consumption which can act as a direct probiotic.

#### 5. PROBABLE ROLE OF SNEHAPANA IN GUT MICROBIOME RESTORATION

**1. Luminal oleation → disruption of dysbiotic biofilms:** Dietary lipids basically coat the intestinal mucosa and loosen the pathogenic biofilms -thus detaching the adherent pathobionts. This mucosal coating of the *Sneha* can be paralleled to the *Nirukti* of the word itself – *Snih preetou*.

**2. Solubilization of lipid soluble toxins:** Most of the endotoxins especially LPS are lipophilic in nature. Hence, the consumed *Sneha* binds to them and mobilizes them in the gut lumen for further evacuation.

**3. Enhancement of Bile secretion:** *Snehapana* mainly enhances bile secretion that has antimicrobial action and promotes only bile metabolizing beneficial bacteria.

**4. Restoration of Epithelial barrier:** *Ghrta* contains butyric acid which is a butyrate analogue that majorly helps in increasing mucus layer thickness and maintaining the tight junction stability.

#### THERAPEUTIC SELECTIVITY IN SHODHANA: Probable rationale for excluding the *Pradhana Karma* of *Vamana*, *Nasya* and *Raktamokshana* from Direct Gut Microbiome Modulation.

**1. Anatomical Basis:** The highest density of gut microbiome can be seen in the distal colon upto  $10^{12}$  CFU per unit area. With respect to *Vamana*, the area of action is mainly the stomach till the 1<sup>st</sup> part of the duodenum. In case of *Nasya*, the area of action is mainly the nasal mucosa, nasopharynx and paranasal sinuses and in case of *Raktamokshana*, it is the vascular blood that is eliminated. Therefore, gastric emptying in *Vamana*, nasal instillation in case of *Nasya* and bloodletting in *Raktamokshana* probably does not directly affect the gut microbiome density and diversity.

**2. Physiological mechanisms:** In case of *Vamana*, large quantities of liquids are administered to the patients, causing distension of the stomach, activation of stretch receptors, reverse peristalsis and retrograde flow of the liquid. Therefore, there is a gastric flush out rather than an intestinal flush out. In case of *Nasya*, only a small amount of *Nasya Dravya* is administered and by the time it gets diffused into systemic circulation and reaches the intestinal lumen, it is highly diluted and in negligible amounts. Whereas since *Nasya Dravya* has direct connection with the CNS through the olfactory pathway, it can modulate the gut microbiome by modulating the gut brain axis. In case of *Raktamokshana*, there is a strong intestinal barrier that does not let the endotoxins present in the intestinal lumen to come in contact with the systemic circulation, hence vascular bloodletting does not cause any significant change in the gut lumen.

**3. Ecological stability of the microbiome:** Even if considered that some amount of local washout of microbiome from the stomach and small intestine in case of *Vamana*, nasal epithelium in case of *Nasya* and vascular anti-inflammatory mechanisms in case of *Raktamokshana* happen, the gut microbiome is said to be the distal microbial reservoir that is said to replenish or reseed any elimination that happens in the GIT. Also, intestinal washout does not have an effect over the biofilms of localized pathobionts present in the respective areas of action of the above procedures.

**4. Evidence from clinical research:** A recent clinical study analysed the stool cultures of patients before and after *Vamana* and checked for *Bacteroides* and *E. coli* counts that were found to be in the normal ranges at both time points.<sup>[110]</sup>

#### COLON- CENTRIC THERAPIES: Probable role of *Virechana* in Gut Microbiome Restoration

Table No.5: Colon- centric therapies: Probable role of *Virechana* in Gut Microbiome Restoration.

| PROBABLE MECHANISMS                                                                                                                                                                                                                        | PARALLELS IN AYURVEDA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Physical (Mechanical) Mechanisms</b> <ol style="list-style-type: none"> <li>1. Accelerated Intestinal Motility and Luminal Clearance</li> <li>2. Disruption of Microbial Biofilms</li> <li>3. Reduction of Intestinal Stasis</li> </ol> | <p><b>Accelerated Intestinal Motility</b> - The following terminologies indicate the role of <i>Virechana</i> in increasing or normalizing the gut motility:</p> <ul style="list-style-type: none"> <li>• <i>Anulomana</i>- <i>Bhitva Bandham Adho Nayet</i>,</li> <li>• <i>Sramsana</i>- <i>Nayatyadha</i> ,</li> <li>• <i>Bhedana</i>- <i>Bhitwa Adha Patayati</i>,</li> <li>• <i>Rechana</i>- <i>Rechayatyapi</i><sup>[11]</sup></li> </ul> <p><b>Luminal clearance, disruption of biofilms, reduction of intestinal stasis:</b></p> <p>The following instances indicate the disruption of adherent pathological biofilms along with their elimination:</p> <ul style="list-style-type: none"> <li>• <i>Sramsana</i>- <i>Shlishtam Koshte Maladhikham Nayatyadha</i>,</li> <li>• <i>Rechana</i>- <i>Maladi Dravatam Nayet</i>,</li> <li>• <i>Tikshna Virechana Dravya Guna</i>- <i>Sukham Kshipram Mahavegam Asaktam Yatpravartate</i>, <i>Antarashayam Akshinvan</i><sup>[11,22]</sup></li> </ul> |
| <b>Chemical Mechanisms</b> <ul style="list-style-type: none"> <li>• Alteration of Luminal pH</li> <li>• Bile Acid–Driven Microbial Selection</li> </ul>                                                                                    | <p><b>Bile acid driven microbial selection and removal of microbial metabolites-</b> The following phrases indicate the '<i>Harana</i>' or elimination of harmful microbial metabolites, hence, justifying the</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

|                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Removal of Microbial Metabolites</li> </ul>                                                                                                                                                                                  | <p>mentioning of <i>Maniki Pramana</i> as a parameter to quantify the <i>Nirhrita Doshas</i>.</p> <ul style="list-style-type: none"> <li><i>Virechana</i>– <i>Adhobhagaharana</i> of <i>Doshas</i>.</li> <li>Order of expulsion of toxins: <i>Vit, Pitta, Kapha, Anila</i><sup>113</sup> - which can be paralleled to the expulsion of endotoxins, secondary bile acids, ammonia, hydrogen sulphide, phenols respectively.</li> </ul>                                                                                                                                                                                                                                                                                 |
| <p><b>Immunological Mechanisms</b></p> <ul style="list-style-type: none"> <li>Interaction with GALT</li> <li>Reduction of Inflammatory Cytokines</li> <li>Restoration of Immune–Microbiome Homeostasis</li> </ul>                                                   | <p><b>The following terminologies and phrases can be correlated to the correction of immune imbalance, enhancing anti-inflammatory pathways in turn strengthening both cell mediated and innate immunity.</b></p> <ul style="list-style-type: none"> <li><i>Malapaham Rogaharam, Vyadhayashcha Upashamyanti, Chiram Jeevayati Anaamayaha</i>.<sup>[114,115]</sup></li> <li>From the preventive point of view: <i>Urdhwam Cha Adhashcha Nityashaha, Rogastatha Na Jayante</i>.<sup>[116]</sup></li> </ul>                                                                                                                                                                                                              |
| <p><b>Ecological and Mucosal Mechanisms</b></p> <ul style="list-style-type: none"> <li>Ecological Reset of Microbial Communities</li> <li>Competitive Recolonization</li> <li>Restoration of Epithelial Barrier Function</li> <li>Mucus Layer Remodeling</li> </ul> | <ul style="list-style-type: none"> <li>The terms like <i>Dhatusthiratvam, Prakrutistheshu Dhatushu</i> which have been mentioned as benefits of <i>Shodhana</i> can be correlated to <i>Virechana</i>'s ability of causing ecological niche stability and making the gut lumen favourable for beneficial bacteria and in turn restoring the intestinal barrier.</li> <li><i>Prakrutishcha Anuvartate</i> can be paralleled to its ability to restore equilibrium by restoring normal diversity and density.</li> <li><i>Chirat Cha Pakam, Jaram Krichrena Labhate</i> can be correlated to a probable ecological reset mechanism that is set in a patient's gut post <i>Virechana</i>.<sup>[117,118]</sup></li> </ul> |
| <p><b>Metabolic Mechanisms</b></p> <ul style="list-style-type: none"> <li>Alteration of Microbial Fermentation</li> <li>Interaction with Host Metabolism</li> </ul>                                                                                                 | <ul style="list-style-type: none"> <li>Terms like <i>Dhatavashcha Abhivardhante</i> indicate stable metabolic pathways leading to a well-nourished gut.</li> <li>One of the <i>Samyak Lakshanas</i> of <i>Virechana</i> is mentioned as <i>Laghutvam Urjo Agnihi</i>, one of the <i>Dhatu-samyak Lakshanas</i> is mentioned as <i>Kayagnirabhivardhate</i>, one of the <i>Shodhana Labha</i> is mentioned as <i>Jwalanasya Deeptim</i> that can be correlated to balanced fermentation patterns and balanced metabolism of all substrates.<sup>119-122</sup></li> </ul>                                                                                                                                               |

### VIRECHANA- AS A ONE SIZE FITS ALL MODALITY TO CORRECT DYSDIOSIS AT EVERY GUT-ORGAN AXES

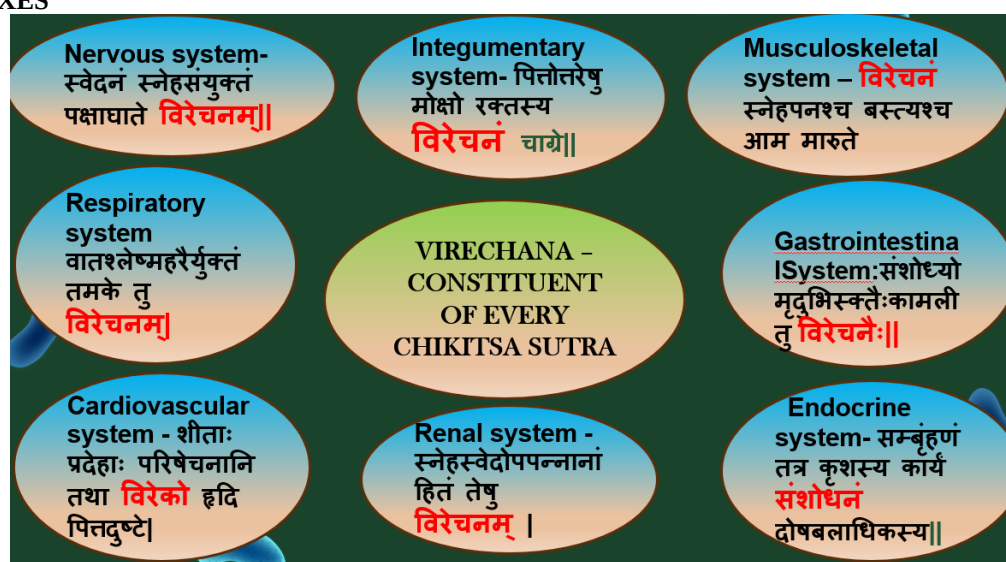


Fig 1: *Virechana*- as a one size fits all modality to correct dysbiosis at every gut-organ axes.

The systemic applicability of *Virechana* described in *Ayurveda* may be explained through its potential role in gut microbiome modulation. *Acharyas* have described the anatomical area of action of *Virechana* as extending

from *Mukha* to *Guda*, encompassing the entire gastrointestinal tract which is considered to be the principal habitat of the human gut microbiome.<sup>123</sup> Since the gut microbiome orchestrates the gut's axes with

literally every organ and organ system, modulation of this common predominating factor provides a plausible scientific basis for the broad therapeutic indications of *Virechana* across multiple organ systems. Thus, *Virechana* may be considered a systemic gut microbiome-modulating intervention, offering a contemporary rationale for its classical description as a constituent of almost every *Chikitsa Sutra* and a potential "one-size-fits-all" approach for diseases associated with gut dysbiosis.

#### **COLON- CENTRIC THERAPIES: Probable role of *Niruha Basti* in Gut Microbiome Restoration.**

**1. COLON AS THE PRIMARY TARGET ORGAN:** Evidence suggests that the largest microbial reservoir of  $10^{11}$ – $10^{12}$  CFU/g is present in the distal part of colon and coincidentally, *Pakwashaya* is considered to be the *Adhishthana* of *Vata*, and *Pakwashaya* & *Amashaya* are considered to be the only 2 *Udbhavasthanas* of a *Vyadhi*. Therefore, *Niruha Basti* can be considered as a colon-targeted bioregulatory intervention affecting the gut microbiome ecosystem.<sup>[124,125]</sup>

**2. FLUID MECHANICS IN THE COLON:** In case of *Niruha Basti*, moderate to large volume of *Niruha Basti Dravya* is administered into the rectum. This causes luminal distension, stretch receptor activation, retrograde flow, generation of shear stress, expulsion of loosely adherent microbes and superficial pathological biofilms due to the transient turbulence caused by the flushing effect of the *Dravya*. This can be considered analogous to quotation of *Acharya Charaka* who quotes that *Basti* causes *Vilodana* of the *Doshas* present in the *Nabhi*, *Kati*, *Parshwa* and *Kukshi Pradesha* and causes optimum *Snehana* of the entire body along with *Purisha* and the vitiated *Doshas* and eliminates them from the body. *Acharya Chakrapani* further comments on the word meaning of *Vilodyate* as *Sankshobhya* i.e., Induction of transient period of discomfort/turbulence/churning effect.<sup>[126]</sup>

**3. REMOVAL OF FECAL MATRIX & ENDOTOXIN LOAD, MOTILITY RESET AND TRANSIT TIME CORRECTION:** The fecal matrix acts as a protective physical scaffold for dysbiosis containing undigested food, microbial biomass, LPS, etc., *Basti* acts as a fecal flush out mechanism removing the source/substrate of dysbiosis. This is supplemented by quotations like *Pavanam Sa Pitta Kapha Vitakam Shuddhikaro Anulomayati Bastihi*. *Acharya Sushruta* metaphorizes this flush-out concept by giving the example of a *Nadi* through which forceful pushing of large quantity of water leads to flush out of all impurities.<sup>[127,128]</sup>

**4. RETENTION PHASE MECHANISMS:** During the retention time/phase of *Niruha Basti Dravya*, there is a shift from flow-dominated to stasis-dominated microenvironment. Mucosal coating & biofilm modulation prevents re-attachment of dislodged

microbes, phytochemical diffusion helps in selective antimicrobial effect therefore, it reprograms microbial composition and function toward symbiosis. It causes an immune reset by removal of immune triggers (fuel for inflammatory pathways), reduction in antigen load, immune system recalibration by barrier restoration & IgA normalization.

#### **5. ECOLOGICAL RESET MECHANISM:**

Dysbiosis is dominated by pathogen dominated biofilms that lead to locked ecosystems and *Niruha Basti* causes the physical disruption of these biofilms by removing the ecological monopoly of pathogenic strains and opens up space for new colonizers. The *Niruha Basti Dravya* acts as a new substrate for beneficial microbes, restores anaerobic gradients & leads to controlled recolonization. Therefore, in a nutshell, *Niruha Basti* leads to destruction of pathological niches + creation of favorable ecological space + guided microbial succession. *Acharya Charaka's* quote in the context of *Basti's* mode of action supplements the concept of targeting only the pathological strains as follows: *Pakwashayam Anupravishya Kevalam Vaikarikam Vatamoolam Chinatti*.<sup>[129]</sup> Several other phrases demonstrate the ecological reset angle of *Niruha Basti's* action such as, *Yashcha Bastim Upaasita Sa Jeevet Sharadaam Shatam*, *Praninaam Amrutopamam*, *Shareeropachaya*, *Varna*, *Bala*, *Arogya*, *Ayushya*.<sup>[130-132]</sup>

#### **6. CONSTITUENT-WISE CONTRIBUTION TO GUT MICROBIOME MODULATION**

***Makshika:*** Components like hydrogen peroxide & phenolic compounds cause biofilm disruption of pathogenic strains, Oligosaccharides selectively feed certain beneficial strains like *Lactobacillus* & *Bifidobacterium*. Polyphenols & flavonoids disrupt bacterial quorum sensing, virulence gene expression and improve the delivery of phytochemicals into biofilms.

***Lavana:*** *Lavana* creates a controlled osmotic gradient that draws water into the intestinal lumen and leads to flushing of toxins. It facilitates mucous layer modulation that removes trapped pathogens and allows better drug penetration. Additionally, sodium ions present in it help in enhanced absorption of other constituents of *Basti* and also consequentially leads to biofilm disruption and motility regulation.

***Sneha:*** Lipids dissolve hydrophobic biofilm layers and cause mucosal repair. Lipid niche creation in the intestinal lumen leads to increased lipid metabolizing bacteria.

***Kalka:*** It contains dietary fibres & resistant plant polysaccharides that act as prebiotic sources. They also showcase a sustained antimicrobial and regulatory action due to the presence of active constituents like alkaloids, tannins, flavonoids, terpenoids.

***Kwatha and Avapa Dravya:*** *Kwatha* contains active components like tannins, glycosides, phenolics that

demonstrate antimicrobial action. *Kwatha* also acts as a solvent for water soluble phytochemicals. *Avapa Dravyas* like *Chatusneha*, *Mamsarasa* in *Vata*, *Kshoudra*, *Ghritha*, *Ksheera* *Sharkara* in *Pitta* and

*Kshara*, *Kshoudra*, *Gomutra* in *Kapha* have prebiotic potential, thus causing selective improvement in diversity of beneficial strains.

**Table No.6: Commonly used Niruha Basti Formulations and their Effect on Gut Microbiome.**

| Formulation                      | Major Phytoconstituents                                              | Effect on Gut Microbiome                                                                                                          |
|----------------------------------|----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| <i>Dashamoola Kashaya Basti</i>  | Flavonoids, tannins, saponins, terpenoids                            | Anti-inflammatory, prebiotic effects, pathogen suppression                                                                        |
| <i>Eradamuladi Niruha Basti</i>  | Ricinoleic acid, fatty acids, alkaloids                              | Strong motility regulator- reduces endotoxin load                                                                                 |
| <i>Takra Basti</i>               | Lactic acid, probiotics, peptides- acts as a probiotic enema         | Direct probiotic replenishment, reduces gut pH (unfavourable for certain pathobionts)                                             |
| <i>Piccha Basti</i>              | Mucilage, polysaccharides, glycyrrhizin                              | Mucosal barrier restoration                                                                                                       |
| <i>Lekhana Basti</i>             | Volatile fatty acids, urea Alkaloids (berberine), tannins, phenolics | Biofilm disruption; antimicrobial; reduces metabolic endotoxemia                                                                  |
| <i>Panchatikta Ksheera Basti</i> | Bitter glycosides, flavonoids, terpenoids, lipids                    | Bitter active principles- antimicrobial & anti-inflammatory, lactose – substrate for lactobacilli                                 |
| <i>Madhutailika Basti</i>        | Oligosaccharides, fatty acids, enzymes                               | Oligosaccharides- prebiotic effect, fatty acids- mucosal integrity maintenance                                                    |
| <i>Mustadi Yapana Basti</i>      | Flavonoids, sterols, polysaccharides, lipids                         | Gut motility, mucosal healing, anti-inflammatory, <i>Mamsa Rasa</i> - amino acids, peptides- nitrogen source- microbial diversity |

**Table No.7: Samyak Nirudha Lakshanas and parallels with gut microbiome.**

| SAMYAK YOGA OF NIRUHA BASTI <sup>[133]</sup> | PARALLELS WITH RESPECT TO EFFECT ON GUT MICROBIOME                                                                                 |
|----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| <i>Prasrishtavinmutrasameeranatvam</i>       | Motility restoration + Transit time normalization + Elimination of dysbiotic substrates.                                           |
| <i>Ruchi</i>                                 | Reduced LPS- ghrelin & vagal signalling back to normal, taste receptor expression normalized.                                      |
| <i>Agnividdhi</i>                            | SCFAs – Butyrate- colonocyte fuel, Acetate & propionate- metabolic regulators, increased enzymatic synergy.                        |
| <i>Ashaya Laghavani</i>                      | Reduction of pathobiont/antigen biomass/load, reduced intraluminal pressure- metabolic state of lightness.                         |
| <i>Rogopashanti</i>                          | Correction of dysbiosis-driven systemic pathology, neurotransmitter regulation, vagal tone enhancement, reduced neuroinflammation. |
| <i>Prakritistatha Cha Balam</i>              | Improves T cell function- reduces inflammation, increases ATP production, SCFA production.                                         |

**PROBABLE ROLE OF ANUVASANA BASTI IN GUT MICROBIOME RESTORATION**  
**LIPID COATING & MUCOSAL BARRIER RESTORATION:** *Sneha Dravya* provides a hydrophobic coating over the mucosa, increases mucous layer thickening, promotes mucin dependent bacteria and in turn strengthens the intestinal barrier. This is justified by the definition of *Sneha Dravya* that highlights its *Kledana Shakti*, the word meaning of *Snigdha*- *Alingana*, *Preeti* and *Mardavakaraka*.

**SELECTIVE ECOLOGICAL MODULATION:** *Anuvasana Basti* acts as a microbiome conditioner as opposed to the cleansing action done by *Niruha Basti*. It acts by supporting beneficial commensal anaerobes and increasing microbial diversity, modulation of anti-

inflammatory action, providing prebiotic & metabolic substrate and improving the quality of gut motility & drug delivery. This concept has been seconded by both *Acharya Charaka* and *Sushruta* who opine that *Anuvasana Basti* is administered with a purpose of causing *Snehana* to the *Srotas* or *Marga* after its *Shodhana* that has been carried out by *Niruha Basti*. Additionally, in the context of assimilation of *Anuvasana Basti Dravya* in the *Pakwashaya*, *Acharya Chakrapani* says that there is an *Avayava* of *Jatharagni* present in the *Pakwashaya* called *Pakwashayopalepaka Agni* that helps in the digestion of the administered *Sneha Dravya*.<sup>[134,135]</sup> Hence, this can also be understood as a component of the functionality of the gut microbiome.

Table No.8: Comparative action of Anuvasana and Niruha Basti over gut microbiome.

| ASPECT                   | ANUVASANA BASTI (SNEHA-BASED)                         | NIRUHA BASTI (KWATHA-BASED)                              |
|--------------------------|-------------------------------------------------------|----------------------------------------------------------|
| PRIMARY ACTION           | Microbiome stabilization & nourishment.               | Microbiome reset & cleansing.                            |
| Effect on microbial load | Preserves and supports existing flora.                | Reduces excess/pathogenic load.                          |
| Ecological role          | Maintains microbial balance (homeostasis).            | Re-establishes microbial equilibrium after disruption.   |
| Mucosal interaction      | Forms protective lipid layer, enhances mucus barrier. | Detaches biofilm & removes adhered toxins/microbes.      |
| Inflammation             | Anti-inflammatory, promotes tolerance.                | Removes pro-inflammatory triggers (ama, endotoxins).     |
| Metabolic effect         | Promotes SCFA production (butyrate support).          | Reduces toxic metabolites, resets fermentation patterns. |
| Motility influence       | Normalizes transit gently (Vata pacification).        | Induces evacuation → motility reset.                     |
| Retention vs elimination | Retained → prolonged microbial modulation.            | Expelled → mechanical + chemical cleansing.              |
| Impact on diversity      | Enhances microbial diversity stability.               | Clears dysbiosis → allows recolonization.                |
| Therapeutic analogy      | “Prebiotic + barrier repair therapy”                  | “Detox + microbiome reset therapy”                       |

#### PROBABLE MODE OF ACTION OF SAMSAJANA KRAMA IN CAUSING DIETARY RECONDITIONING OF THE GUT

**PHASE 1: MICROBIAL REDUCTION AFTER SHODHANA (CONTROLLED MICROBIAL DEPLETION):** After *Virechana* or *Niruha Basti*, the gut undergoes a multi layered depletion event that can be interpreted not just as a mechanical evacuation of luminal contents but further, as a biological reset. After *Shodhana*, luminal microbes are washed out with faecal matter, biofilm associated bacteria are partially dislodged from the mucosa, certain metabolites like endotoxins and bile derivatives are flushed out along with several inflammatory microbial products. Functional consequences include reduced microbial density, reduced metabolic activity, reduced fermentation pressure and endotoxin burden that creates a low-profile biochemical

environment in the gut in turn preparing the gut for the further phases of stepwise recolonization.

**PHASE 2: NICHE CREATION AND MICROBIAL RECOLONIZATION:** Post completion of *Shodhana*, there is a creation of an ecological niche space in the gut that acts as a window for directed microbial re-assembly. Pre- *Shodhana* a microbe would have occupied a particular nutrient, spatial and metabolic niche or role. Post *Shodhana*, many niches become vacant, under occupied or weakly competitive. During this critical window, several microbiological processes are activated wherein there is a clear loss of competitive exclusion and an opportunity for early colonizers to determine the future microbiome pattern. This can be supplemented by the quotations of our *Acharyas* who opine that the *Shareera* attains an *Avastha* of *Mandagni* post completion of *Shodhana*.<sup>[136]</sup>

Table No.9: Probable mode of Action of Samsarjana Krama Over Gut Microbiome.

| NAME OF THE AHARA KALPANA | INGREDIENTS                                           | NUTRIENT PROFILE                                                        | EFFECT ON MICROBIOME                                                                                                                                                                                             |
|---------------------------|-------------------------------------------------------|-------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PEYA                      | <i>Tandula: Jala- 1:14- Siktayukta</i>                | Carbohydrates (Amylose, Amylopectin)                                    | HOLDING PHASE/TRANSITIONAL ECOSYSTEM BEFORE RECOLONIZATION: Due to absence of a strong substrate, it is acted upon by mild saccharolytic bacteria. This phase gives rise to a stabilized low density microbiome. |
| VILEPI                    | <i>Tandula: Jala- 1:4- Viraladrava- semi solid</i>    | Carbohydrates(Amylose, Amylopectin)- less diluted higher starch density | QUISCENT TO ACTIVELY REORGANIZING ECOSYSTEM Selective expansion of saccharolytic bacteria. Initial colonization occurs and controlled fermentation begins.                                                       |
| AKRITA YUSHA              | <i>Shimbidhanya- Mudga, Masha, Masura+ Jala- 1:18</i> | Amino acids, peptides, residual starch, oligosaccharides                | EARLY COLONIZING MICROBIOME TO METABOLICALLY INTEGRATED ECOSYSTEM: Introduction of nitrogen rich substrate                                                                                                       |

|                   |                                                                                                               |                                                                                         |                                                                                                                                                                                                                                                    |
|-------------------|---------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   |                                                                                                               |                                                                                         | acts as bridge between carbohydrate metabolism to mixed metabolism. An increased bifidobacterium density maybe found.                                                                                                                              |
| KRITA YUSHA       | <i>Shimbidhanya- Mudga, Masha, Masura+ Jala- 1:18 + Sneha + Prakshepaka Dravyas(Shunti, Maricha, Pippali)</i> | Amino acids, peptides, residual starch, oligosaccharides, medium chain fatty acids      | METABOLICALLY INTEGRATED TO FUNCTIONALLY OPTIMIZED ANTI INFLAMMATORY ECOSYSTEM: Increased firmicutes ( butyrate producers) are seen along with stronger metabolic output.                                                                          |
| AKRITA MAMSA RASA | <i>Mamsa: Jala – 1:8 reduced to 1/4<sup>th</sup></i>                                                          | Amino acids, peptides, collagen derived components, micronutrients- Fe, Zn              | FUNCTIONALLY OPTIMIZED TO HOST SUPPORTIVE ECOSYSTEM : There is presence of controlled proteolytic substrates, increased alpha diversity and a balance between proteolytic and saccharolytic substrates for the microbial succession to take place. |
| KRITA MAMSA RASA  | <i>Mamsa: Jala – 1:8 reduced to 1/4<sup>th</sup> + Sneha + Prakshepaka Dravyas(Shunti, Maricha, Pippali)</i>  | Amino acids, peptides, fatty acids, collagen derived components, micronutrients- Fe, Zn | HOST SUPPORTIVE ECOSYSTEM TO STABLE MAXIMAL DIVERSE STRONG OUTPUT ECOSYSTEM: There is an increased alpha diversity and full spectrum metabolic substrate present at this phase.                                                                    |

Finally, the patient is instructed to revert back to *Sadharana Ahara* after 3,5 or 7 days based on the type of *Shuddhi* where they are encouraged to start consuming a normal balanced diet. Recent studies have demonstrated that a traditional Indian thali provides a wide range of microbiota-modulating nutrients that collectively promote gut health. Dal supplies microbiota-accessible carbohydrates (MACs), dietary fibre, and polyphenols that enrich *Bifidobacterium* and *Prevotella* while increasing short-chain fatty acid (SCFA) production. Curd, buttermilk, and fermented pickles provide probiotic bacteria and organic acids that inhibit pathogens and enhance immune homeostasis. Rice and roti serve as sources of resistant starch that sustain SCFA production, whereas vegetable curries, leafy vegetables, rasam, and sambar provide polyphenols, carotenoids, flavonoids, and organosulphur compounds that promote beneficial bacteria, reduce inflammation and improve microbial diversity. Collectively, these dietary components support intestinal barrier integrity, immune regulation and metabolic health through favourable modulation of the gut microbiota.<sup>[137]</sup>

Therefore, in a nutshell, *Samsarjana Krama* leads to microbial succession in 3 stages viz., Stage 1: Pioneer Colonizers, Stage 2: Secondary Fermenters and Stage 3: Stable anerobic community. This has been aptly metaphorized by *Acharya Charaka* who opines that similar to kindling a small fire with *Trina, Gomaya* etc., *Peyadi Samsarjana* successfully kindles and stimulates the *Jatharagni* and makes it *Mahan, Sthira* and capable of digesting all types of substrates.<sup>[138]</sup>

## CONCLUSION

The gut microbiome is fundamental to human health, while its disruption (dysbiosis) contributes to the pathogenesis of numerous diseases, validating both the *Ayurvedic* principle "*Rogaha Sarvepi Mandagnau*" and Hippocrates's view that says "all disease begins in the gut." *Panchakarma* may therefore be viewed as a systematic approach to restoring gut microbial homeostasis, wherein *Pachana Deepana* removes the nutritional substrate for dysbiosis, *Snehapana* mobilizes toxins and microbial biofilms, *Virechana* eliminates pathogenic microbes and inflammatory metabolites, *Niruha Basti* resets the colonic microbial ecosystem, and *Anuvasana Basti* restores mucosal integrity and microbial balance. Future research should validate these effects through  $\alpha$ - and  $\beta$ -diversity analyses, metagenomics, SCFA profiling and evaluation of microbiome changes in relation to *Shodhana* procedures, *Basti* retention time and dosage to establish evidence-based mechanisms of *Panchakarma*.

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