

## Takra (Ayurvedic Buttermilk) as a Microbiota-Directed Functional Food: A Systematic Review of Mechanistic Pathways and Clinical Implications

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Cite this paper as: Dr. Krutika S. Chaudhary, Dr. Suhas A. Chaudhary, Dr. Rahul K. Shingadiya (2024) Takra (Ayurvedic Buttermilk) as a Microbiota-Directed Functional Food: A Systematic Review of Mechanistic Pathways and Clinical Implications..*Frontiers in Health Informatics, Vol.13, No.6, 4778-4787*

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### ABSTRACT:

**Background:** Takra (Ayurvedic buttermilk) is a classical fermented dairy preparation extensively described in Ayurvedic literature for the management of Grahani, Atisara, Arsha, and metabolic disorders. Emerging microbiome research suggests that fermented dairy products exert significant effects on gut microbial ecology, immune modulation, and metabolic signalling.

**Objective:** To systematically review available evidence regarding microbiota-modulating effects of Takra and fermented buttermilk preparations and to correlate modern mechanistic findings with classical Ayurvedic concepts.

**Methods:** A systematic search of PubMed, Scopus, and Web of Science databases was conducted for studies published between January 2000 and January 2024 using predefined keywords related to fermented dairy, gut microbiota, SCFAs, immune regulation, and intestinal barrier function. Human clinical studies, animal experiments, and in vitro investigations were included.

**Results:** Fermented buttermilk preparations significantly enhanced beneficial microbial taxa, including *Lactobacillus* spp., *Bifidobacterium* spp., and *Faecalibacterium prausnitzii*, while reducing Proteobacteria and Enterobacteriaceae overgrowth. Increased SCFA production, improved intestinal barrier integrity, suppression of NF- $\kappa$ B-mediated inflammation, and modulation of bile acid-FXR/TGR5 pathways were consistently reported. Gut-brain axis regulation and psychobiotic effects were also observed.

**Conclusion:** Takra demonstrates multidimensional microbiota-mediated therapeutic potential that aligns closely with Ayurvedic principles of Deepana, Pachana, Grahi, and Vata-Kaphashamana. Integrating traditional Ayurvedic fermented dietary therapeutics with modern microbiome science may provide novel preventive and therapeutic approaches for gastrointestinal, metabolic, inflammatory, and neuropsychological disorders...

### INTRODUCTION

The human gastrointestinal tract harbours a highly complex and dynamic microbial ecosystem that plays a central role in digestion, nutrient assimilation, immune regulation, metabolic signalling, and maintenance of intestinal homeostasis. Recent advances in microbiome science have demonstrated that alterations in gut microbial composition and function, commonly termed dysbiosis, are associated with a broad spectrum of disorders, including inflammatory bowel disease, irritable bowel syndrome, obesity, diabetes mellitus, neuropsychiatric illnesses, allergic disorders, and colorectal cancer. Consequently, dietary interventions capable of modulating the gut microbiota are increasingly recognised as promising therapeutic and preventive strategies in modern medicine. Among such interventions, fermented foods have gained considerable scientific attention due to their ability to deliver beneficial microorganisms, bioactive metabolites, and immunomodulatory compounds that influence host-microbe interactions.

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Fermented dairy products constitute one of the most extensively studied categories of functional foods. These preparations are rich in lactic acid bacteria (LAB), peptides, vitamins, exopolysaccharides, and fermentation-derived metabolites that contribute to improved gut microbial diversity and intestinal barrier integrity. Experimental and clinical studies have shown that fermented dairy consumption can enhance populations of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, increase production of short-chain fatty acids (SCFAs), reduce intestinal inflammation, and modulate mucosal immune responses. Emerging evidence further indicates that microbial metabolites derived from fermented foods interact with host signalling pathways, including nuclear factor-kappa B (NF- $\kappa$ B), Toll-like receptors (TLRs), bile acid receptors such as farnesoid X receptor (FXR) and Takeda G-protein receptor 5 (TGR5), thereby influencing systemic metabolic and inflammatory processes

Within the traditional Indian system of Ayurveda, Takra (Ayurvedic buttermilk) occupies a unique position as both a dietary preparation and a therapeutic agent. Classical Ayurvedic compendia, including the Charaka Samhita, Ashtanga Hridaya, and Sushruta Samhita, describe Takra as an important formulation possessing Deepana (enhancement of digestive fire), Pachana (improvement of digestion and metabolism), Grahi (absorbent and bowel-regulating), and Tridosha-balancing properties.<sup>i</sup> It is traditionally indicated in disorders such as Grahani (malabsorption syndrome), Atisara (diarrhoea), Arsha (haemorrhoids), inflammatory gastrointestinal diseases, obesity, and metabolic dysfunctions.<sup>ii</sup> Ayurveda also emphasises that Takra prepared through appropriate fermentation and churning processes possesses superior digestibility and therapeutic efficacy compared to unfermented milk products.<sup>iii</sup> Such traditional observations appear increasingly relevant in the context of contemporary microbiome research.

Modern scientific investigations suggest that fermented buttermilk preparations contain diverse probiotic microorganisms and bioactive metabolites capable of influencing gut ecology and host physiology.<sup>iv</sup> Fermentation-derived lactic acid bacteria may contribute to restoration of microbial balance, enhancement of mucosal barrier function, suppression of pathogenic bacteria, and regulation of inflammatory cytokines. Furthermore, metabolites such as SCFAs—including acetate, propionate, and butyrate—play crucial roles in epithelial energy metabolism, tight junction integrity, immune tolerance, and gut–brain communication.<sup>v</sup> These microbiota-mediated mechanisms closely resemble the Ayurvedic conceptual framework of restoring Agni (digestive and metabolic capacity), maintaining intestinal stability, and preventing Ama formation, which is considered a pathogenic factor in many diseases.<sup>vi</sup>

Despite growing global interest in functional foods and microbiome therapeutics, Takra remains insufficiently explored in contemporary biomedical literature. Existing evidence is scattered across studies on fermented dairy products, probiotics, intestinal inflammation, and metabolic regulation, with limited efforts to integrate these findings within the Ayurvedic perspective. Moreover, mechanistic pathways linking Takra consumption to microbiota modulation, intestinal permeability, immune regulation, and metabolic signalling have not been systematically synthesised.<sup>vii</sup> Bridging traditional Ayurvedic knowledge with modern microbiome science may provide important insights into low-cost, culturally acceptable, and evidence-based dietary therapeutics.

Therefore, the present systematic review aims to critically evaluate available evidence regarding Takra and fermented buttermilk preparations in relation to gut microbiota modulation and associated molecular, metabolic, and immunological mechanisms. The review further seeks to correlate emerging microbiome findings with classical Ayurvedic concepts and to explore the potential clinical implications of Takra in gastrointestinal, metabolic, inflammatory, and neuropsychological disorders.

## METHODS

### Search Strategy

A systematic literature review was conducted to evaluate the effects of Takra and fermented buttermilk preparations on gut microbiota modulation, intestinal barrier integrity, inflammatory pathways, and metabolic regulation. Electronic databases including PubMed, Scopus, and Web of Science were systematically searched for relevant studies published between January 2000 and January 2024.

The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to fermented dairy products, microbiota, immune regulation, and metabolic signaling. The following search terms and Boolean combinations were used:

“buttermilk AND microbiota”

“fermented dairy AND SCFA”

“lactic acid bacteria AND intestinal barrier”

“probiotics AND NF- $\kappa$ B”

“fermented milk AND metabolic syndrome”

Additional manual screening of reference lists from eligible studies was also performed to identify potentially relevant articles not retrieved through the primary database search. Duplicate records were removed before the screening process. Titles and abstracts were independently screened for relevance, followed by full-text assessment of eligible studies.

#### **Inclusion Criteria**

Studies were included in the review if they met the following criteria:

Human clinical trials evaluating fermented buttermilk, probiotic dairy products, or Takra-related interventions.

Animal experimental studies investigating mechanistic pathways associated with gut microbiota modulation, immune regulation, or intestinal barrier function.

In vitro microbiome or cellular studies examining effects of fermented dairy components, lactic acid bacteria, or microbial metabolites.

Studies reporting outcomes related to gut microbiota composition, short-chain fatty acid (SCFA) production, inflammatory cytokines, intestinal permeability, or metabolic parameters.

Articles published in peer-reviewed journals between January 2000 and January 2025.

#### **Exclusion Criteria**

Studies were excluded if they met any of the following conditions:

Studies involving non-fermented dairy products without probiotic or fermentation-related interventions.

Narrative reviews, systematic reviews, editorials, commentaries, conference abstracts, or articles lacking primary experimental or clinical data.

Non-English language publications.

Studies with insufficient methodological details or unavailable full text.

Articles unrelated to microbiota-mediated mechanisms or gastrointestinal/metabolic outcomes.

#### **Data Extraction**

Data extraction was independently performed using a standardized extraction format. Relevant variables obtained from each eligible study included:

Study design and sample characteristics

Type of fermented dairy or buttermilk intervention

Microbial diversity indices and relative abundance of bacterial taxa

Short-chain fatty acid (SCFA) concentrations

Cytokine and inflammatory marker levels

Intestinal permeability and tight junction protein expression

Metabolic parameters including glucose regulation, lipid profile, and body weight changes

Duration of intervention and major clinical outcomes

Extracted findings were qualitatively synthesized to identify common mechanistic pathways linking fermented buttermilk preparations with microbiota modulation, immune regulation, and metabolic health outcomes

## **RESULTS**

### **Microbial Composition Modulation**

The reviewed studies consistently demonstrated that fermented buttermilk preparations positively influence gut microbial composition and diversity.<sup>viii</sup> Human clinical trials, animal studies, and in vitro investigations reported a significant increase in beneficial bacterial populations including *Lactobacillus* spp., *Bifidobacterium* spp., and *Faecalibacterium prausnitzii* following administration of fermented dairy products.<sup>ix</sup> These microbial taxa are known for their anti-inflammatory activity, SCFA production, and maintenance of intestinal homeostasis.<sup>x</sup>

Conversely, fermented buttermilk interventions were associated with a reduction in potentially pathogenic microbial groups, particularly members of the phylum Proteobacteria and excessive growth of Enterobacteriaceae.<sup>xi</sup> Several human intervention trials reported significant improvement in alpha diversity indices, indicating restoration of microbial richness and ecological balance within the gut microbiome.<sup>xii</sup>

From an Ayurvedic perspective, these findings may correlate with the concept of *Ama pachana*, wherein restoration of healthy digestive and metabolic processes leads to normalization of intestinal function and reduction of pathological accumulation of *Ama*.<sup>xiii</sup>

### SCFA Production and G-Protein Coupled Receptor Signaling

Multiple studies demonstrated that fermentation-derived metabolites from buttermilk significantly enhance the production of major short-chain fatty acids (SCFAs), including butyrate, propionate, and acetate.<sup>xiv</sup> Among these metabolites, butyrate emerged as a central mediator of intestinal and systemic health benefits.<sup>xv</sup>

Mechanistic studies revealed that butyrate activates G-protein coupled receptors including GPR41 and GPR43, while simultaneously stimulating AMP-activated protein kinase (AMPK) signaling pathways.<sup>xvi</sup> In addition, butyrate exerts epigenetic effects through inhibition of histone deacetylases (HDACs), thereby modulating inflammatory gene expression.<sup>xvii</sup>

These molecular actions collectively contribute to increased differentiation of regulatory T cells (Tregs), suppression of pro-inflammatory cytokines such as IL-6 and TNF- $\alpha$ , and enhancement of epithelial regeneration and mucosal repair processes.<sup>xviii</sup> The observed immunometabolic effects support the traditional Ayurvedic attributes of Takra in maintaining digestive stability and intestinal resilience.<sup>xix</sup>

### Intestinal Barrier Integrity

Several preclinical and clinical studies indicated that fermented dairy products improve intestinal barrier integrity through modulation of epithelial tight junction proteins and mucosal defence mechanisms.<sup>xx</sup> Fermented buttermilk supplementation significantly increased expression of occludin and zonula occludens-1 (ZO-1), both of which are critical for maintaining epithelial barrier function.<sup>xxi</sup> Enhanced mucin production was also observed, contributing to improved mucosal protection against luminal pathogens and toxins.<sup>xxii</sup>

In parallel, studies reported reduced lipopolysaccharide (LPS) translocation and lower levels of systemic endotoxemia, suggesting decreased intestinal permeability. Mechanistically, these effects were mediated primarily through SCFA-induced AMPK activation and inhibition of NF- $\kappa$ B-dependent inflammatory signalling pathways.<sup>xxiii</sup>

These observations closely resemble the Ayurvedic principle of *Grahani sthirikarana*, which emphasizes restoration and stabilization of intestinal integrity and absorptive function.<sup>xxiv</sup>

### Immune Modulation

Lactic acid bacteria (LAB) strains isolated from fermented dairy products demonstrated significant immunomodulatory activity across multiple experimental models.<sup>xxv</sup> Fermented buttermilk interventions were associated with increased production of anti-inflammatory cytokines such as IL-10, along with reduction of pro-inflammatory mediators including TNF- $\alpha$  and IL-17.<sup>xxvi</sup> Enhancement of secretory immunoglobulin A (sIgA) production was also consistently reported, indicating improved mucosal immune defence.<sup>xxvii</sup>

These immunological effects appear particularly relevant in inflammatory and immune-mediated disorders, including inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), haemorrhoids, and various dermatological conditions associated with gut dysbiosis.<sup>xxviii</sup> Collectively, the findings suggest that Takra-derived microbial metabolites and probiotic organisms contribute to immune homeostasis through modulation of both innate and adaptive immune responses.<sup>xxix</sup>

### Metabolic Regulation via Bile Acid Pathways

Emerging evidence from mechanistic studies demonstrated that fermented dairy-associated microorganisms possess bile salt hydrolase activity capable of altering bile acid metabolism and downstream metabolic signalling pathways.<sup>xxx</sup> These microbial transformations influence farnesoid X receptor (FXR) signalling and activation of Takeda G-protein receptor 5 (TGR5), leading to enhanced glucagon-like peptide-1 (GLP-1) secretion and improved insulin sensitivity.<sup>xxxi</sup>

Clinical and experimental studies further reported improvements in glycemic regulation, lipid metabolism, and inflammatory biomarkers following fermented dairy consumption.<sup>xxxii</sup> These findings indicate that microbiota-mediated bile acid signalling may represent an important mechanism underlying the therapeutic potential of Takra in metabolic disorders.<sup>xxxiii</sup>

### Gut-Brain Axis

Several studies highlighted the role of fermented dairy-induced microbiota modulation in regulating the gut-brain axis.<sup>xxxiv</sup> Changes in microbial composition influenced tryptophan metabolism, serotonin biosynthesis, gamma-aminobutyric acid (GABA) production, and hypothalamic-pituitary-adrenal (HPA) axis activity involved in cortisol regulation.<sup>xxxv</sup>

These neurochemical and endocrine alterations were associated with improvements in anxiety, depressive symptoms, stress-related gastrointestinal dysfunction, and irritable bowel syndrome accompanied by

psychological manifestations.<sup>xxxvi</sup> The reviewed evidence suggests that Takra and related fermented preparations may exert psychobiotic effects through bidirectional communication between the gut microbiota and central nervous system.<sup>xxxvii</sup>

## DISCUSSION

The findings of the present systematic review indicate that Takra and fermented buttermilk preparations exert broad-spectrum microbiota-modulating effects through interconnected microbial, metabolic, immunological, and epithelial pathways.<sup>xxxviii</sup> The observed enhancement of beneficial bacterial populations, increased short-chain fatty acid (SCFA) production, stabilization of intestinal barrier integrity, and suppression of inflammatory signaling collectively support the therapeutic potential of Takra as a microbiota-directed functional food.<sup>xxxix</sup> Importantly, these modern mechanistic observations demonstrate remarkable conceptual convergence with classical Ayurvedic descriptions of Takra found in traditional texts such as the Charaka Samhita and Ashtanga Hridaya.

Ayurveda describes Takra as possessing *Deepana*, *Pachana*, *Grahi*, and *Vata-shamaka* properties, each of which appears to correspond to identifiable physiological and microbiological mechanisms.<sup>xl</sup> The *Deepana* action, traditionally interpreted as stimulation of digestive fire (*Agni*), may be understood in modern terms as enhancement of microbial enzymatic activity and optimization of digestive metabolism.<sup>xli</sup> Fermentation-derived lactic acid bacteria improve breakdown of dietary substrates, promote nutrient bioavailability, and enhance microbial metabolic efficiency within the gut ecosystem.<sup>xlii</sup>

Similarly, the *Pachana* property of Takra, associated with digestion and elimination of *Ama* (metabolic toxins or incompletely processed metabolites), may correlate with SCFA-mediated metabolic regulation and detoxification pathways.<sup>xliii</sup> Increased production of butyrate, acetate, and propionate contributes to improved epithelial energy metabolism, regulation of inflammatory cascades, and maintenance of intestinal homeostasis.<sup>xliv</sup> SCFA-mediated activation of GPR41, GPR43, and AMPK signalling pathways further supports efficient metabolic processing and immune regulation, thereby resembling the Ayurvedic concept of correction of impaired digestion and metabolism.<sup>xliv</sup>

The classical *Grahi* effect of Takra, traditionally associated with improved intestinal absorption and stabilization of bowel function, is strongly reflected in the observed enhancement of tight junction proteins, including occludin and ZO-1.<sup>xlvi</sup> Reduction in intestinal permeability and endotoxin translocation suggests restoration of epithelial integrity and mucosal defence mechanisms. These findings are particularly relevant in conditions such as irritable bowel syndrome, inflammatory bowel disease, chronic diarrhoea, and malabsorption syndromes, where intestinal barrier dysfunction is a central pathological feature.<sup>xlvii</sup>

The *Vata-shamaka* property described in Ayurveda may also be interpreted through modern anti-inflammatory and neuroimmune mechanisms.<sup>xlviii</sup> Gut dysbiosis and intestinal inflammation are increasingly linked with altered gut motility, visceral hypersensitivity, stress responses, and neuropsychological symptoms.<sup>xlix</sup> Fermented buttermilk-induced reduction in inflammatory mediators such as TNF- $\alpha$ , IL-6, and IL-17, along with modulation of the gut-brain axis, suggests potential relevance in disorders involving gut inflammation and functional gastrointestinal disturbances traditionally associated with aggravated *Vata dosha*.

Another important observation emerging from the review is the role of fermented dairy microorganisms in bile acid metabolism and metabolic signalling. Activation of FXR and TGR5 pathways, enhanced GLP-1 secretion, and improved insulin sensitivity suggest that Takra may possess therapeutic implications beyond gastrointestinal disorders, particularly in obesity, metabolic syndrome, and type 2 diabetes mellitus.<sup>l</sup> These findings align with increasing global interest in food-based microbiome therapeutics capable of influencing systemic metabolic health through non-pharmacological interventions.

Despite promising evidence, several limitations remain. Considerable heterogeneity exists among available studies regarding microbial strains, fermentation methods, dosage, duration of intervention, and outcome measures. Direct studies specifically evaluating classical Ayurvedic Takra preparations are limited, and many available data are extrapolated from broader fermented dairy research. Furthermore, high-quality randomized controlled trials incorporating advanced microbiome sequencing, metabolomics, and systems biology approaches remain insufficient.

Overall, the convergence of Ayurvedic principles and contemporary microbiome science suggests that Takra may be regarded as a functional microbiota-directed dietary therapy with significant translational potential. Integrating

traditional fermented dietary practices with modern microbiome research may open new avenues for preventive and therapeutic strategies targeting gastrointestinal, metabolic, inflammatory, and neuropsychological disorders

## CONCLUSION

The present systematic review highlights the emerging scientific relevance of Takra as a microbiota-modulating functional food with multidimensional therapeutic potential. Evidence from preclinical, mechanistic, and clinical studies demonstrates that fermented buttermilk preparations beneficially influence gut microbial composition, enhance short-chain fatty acid production, strengthen intestinal barrier integrity, regulate inflammatory and immune pathways, and improve metabolic signalling. These biological effects collectively contribute to the restoration of intestinal homeostasis and systemic health.

Importantly, the identified molecular and microbiological mechanisms show remarkable concordance with classical Ayurvedic concepts describing Takra as *Deepana*, *Pachana*, *Grahi*, and *Vata-shamaka*. Enhancement of microbial enzymatic activity parallels the *Deepana* effect, SCFA-mediated metabolic regulation reflects *Pachana*, stabilization of tight junction proteins corresponds to *Grahi*, and suppression of inflammatory pathways aligns with *Vata-shamana*. Such convergence between traditional Ayurvedic wisdom and contemporary microbiome science provides a strong conceptual framework for understanding the therapeutic significance of Takra in modern biomedical terms.

The review further suggests that Takra may possess broad clinical applicability in gastrointestinal, metabolic, inflammatory, and neuropsychological disorders through microbiota-mediated pathways involving SCFA signaling, bile acid metabolism, immune modulation, and gut-brain axis regulation. Given its cultural acceptability, low cost, nutritional value, and therapeutic versatility, Takra represents a promising candidate for microbiota-directed dietary interventions and integrative healthcare approaches.

However, despite encouraging evidence, significant gaps remain in the current literature. Standardized studies evaluating classical Ayurvedic Takra formulations are limited, and considerable heterogeneity exists in fermentation methods, microbial strains, intervention protocols, and outcome assessments. Future research should therefore focus on well-designed randomized controlled trials incorporating advanced microbiome sequencing, metabolomics, transcriptomics, and systems biology approaches to validate traditional claims and establish evidence-based therapeutic guidelines.

In conclusion, Takra emerges as a scientifically relevant functional fermented food that bridges ancient Ayurvedic dietary therapeutics with modern microbiome research. Its integration into contemporary preventive and therapeutic strategies may offer novel opportunities for safe, sustainable, and holistic management of chronic gastrointestinal and metabolic disorders.

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