

# Microbiome-Mediated Pharmacognosy: A New Paradigm to Drug Discovery

Sharmistha Basu

Assistant Professor, Department of Botany, Victoria Institution (College),  
78-B A.P.C. Road, Kolkata 700009

## Abstract

The science of life which is more than 3000 years old – ‘Ayurveda’, is vital for maintaining holistic health by balancing body, mind and soul through personalised and natural preventive care methods. Ayurveda emphasizes in identifying the root cause of illness rather than just treating the symptoms, for promoting long-term wellness. Ancient, fermented formulations like Asava, Arishta, Takra, and Kanji can convert plant glycosides into aglycones and generate postbiotic molecules which can enhance preservation and drug delivery under alcoholic media. The present article is the amalgamation of classical Ayurvedic knowledge with the modern techniques like Pharmacometagenomics, metabolomics, and functional bioassays, highlighting the importance of microbiome mediated pharmacognosy. There are research gaps in quantity, fermentation, microbiome, mapping, postbiotic molecular characterisation and clinical relation of fermented formulation effects on human gut ecology. However, by bridging the gap between the modern science and the traditional wisdom, a fermentation model can be created, which can be treated as a model system for developing the next generation, therapeutics for enhanced bioavailability, targeted gut modulation, and novel antimicrobial strategies

**Keywords:** Pharmacometagenomics, Sandhana Kalpana, post biotic, fermentation model, Biotransformation; Metabolomics.

## 1. Introduction

Trillions of microorganisms harbouring in our body called microbiome play the most important role in immune modulation, disease pathogenesis, and drug metabolism. Research works done in the area of metagenomics, metabolomics, and Systems Biology have beautifully shown that how the gut microbiota actively transforms these dietary phytochemicals and pharmaceutical compounds into metabolites, which can be significantly different from their parent molecules (Mani et al., 2025; Singh et al., 2020) This remarkable biotransformation not only happens in the human gastrointestinal tract, but also within the plant tissues where endophyte microorganisms provide suitable environment for the biosynthesis of secondary metabolites, which determines the therapeutic properties of the plant (Santhosh kumar et al., 2025; Singh, 2023; Yadav, 2025). There are diverse applications of microbiome-mediated phytochemical transformation. Firstly, aglycones produced by microbial conversion of glycosides greatly

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enhances the bioavailability and alters pharmacokinetic profiles which is demonstrated by the gut microbial conversion of mangiferin to norathyriol. This exhibits distinct effects on short chain fatty acid metabolism, and gut pH (Bunt et al., 2025). Second, postbiotics generated after fermentation are crucial bioactive molecules which are released from microorganisms and exerts, immunomodulator, antioxidant, antimicrobial, and anti-inflammatory effects independent of live microbial cells (Żółkiewicz et al., 2020; Park et al., 2022; Scott et al., 2022). third secondary metabolites, which are produced by the end of microorganisms significantly contributes to the plants therapeutic chemistry providing sustainable alternative to plant harvest for drug production (Santhosh kumar et al., 2025; Singh, 2023; Mitra et al., 2021).

Ayurvedic formulation like Asava and Arishta are alcohol-aqueous extractions which shows enhanced shelf-life, improved solubility of active constituents and often with greater therapeutic values (Samuel et al., 2024). Also, fermented preparations like Takra (medicated buttermilk) and Kanji (fermented cereal beverages) provide both transformed phytochemicals and probiotic or postbiotic components that are beneficial to gut microbiome, composition, and function (Santhosh kumar et al., 2025; Żółkiewicz et al., 2020). This article represents the microbiome-mediated pharmacognosy, which is based on the synthesis of traditional Ayurvedic fermentation knowledge with contemporary microbiome science and aims to explain how the use of traditional fermentation knowledge can guide the development of next generation therapeutics that utilise microbial transformation for increased efficacy, unique mechanism of action and targeted delivery of therapeutics.

## 2. Traditional Formulations (Sandhana Kalpana)

Asava–Arishta (alcoholic), Takra (dairy lactic), and Kanji (cereal/vegetable acidic) are some distinct related fermentative strategies.

### 2.1 Alcoholic Fermentations: Asava and Arishta

When fresh juices or cold infusions are fermented with added sugars and natural starters, like the Dhataki (*Woodfordia fruticosa*), Asava and Harta are produced. These are self generated alcoholic poly herbal formulations (Sekar & Vinothkanna, 2019; Vidhu & Prerna, 2019; Das & Das, 2019). Presence of ethanol ( ~5–12% v/v) increases the extraction of hydrophilic and lipophilic acts which acts as an intrinsic preservative, as well as it improves the absorption, pliability, and shelf life (Sekar & Vinothkanna, 2019; Sharma et al., 2024; Panda et al., 2022; Vidhu & Prerna, 2019; M et al., 2024). While the classical texts guide us about the type of container to be used, standardised substrates (Phala, Dhanya, Mula, etc.), duration, temperature, and end point test, the modern research, developments and techniques projects, physio, chemical profile process, optimisation, microbial characterisation, and GMP oriented quality control (Vidhu & Prerna, 2019; Pant et al., 2021; Divya et al., 2021). For metabolic, digestive, respiratory and cardiovascular disorders, Asava–Arishta are widely used and the most common examples which are been studied are Drakshasava, Vasakasava, Tambulasava, Beejakarishtha and Vidangarishta (Panda et al., 2022; Vidhu & Prerna, 2019; M et al., 2024).

### 2.2 Fermented Buttermilk Preparations: Takra

Takra belongs to Sandhana Kalpana, but it is a lactic acid fermentation within a dairy substrate,

produced from churned butter milk with proper dilution and flavouring (Divya et al., 2021). Though less research work has been done on Takra, ancient literature mentions that Takra is a therapeutic food /medicine for metabolic gut disturbances, Adema, Grahana, and Arisha as, the lightness, sourness and the probiotic properties of these drinks are helpful for the gut health (Divya et al., 2021). The beneficial qualities of this lactic acid preparation are mainly attributed to the altered milk, proteins, organic acids and the friendly lactic acid bacteria which improves the digestion and links Takra conceptually to the contemporary probiotic buttermilk.

### 2.3 Kanji: Cereal and Vegetable Fermentations

Popularly known as Dhanyamla, Kanjika, Aranala), Kanji is categorised under Shukta Kalpana (acidic fermentations) within Sandhana Kalpana (Kamatar et al., 2024) Kanji is prepared using cereals or vegetables (carrots, beetroot), water and various types of spices. Fermentation results in a very delicious drink with low alcoholic content ( $\approx 1\%$  v/v) rich in organic acids with pH approximately 3.4 to 3.5 and with low viscosity. Recent research work shows that the choice of the pots – mud pots and plastic containers yield significantly, similar physicochemical profiles of the drink. However, organoleptics (odor) may vary, the importance of careful choice of containers for patient acceptability. Thus, Kanji is a mildly acidic digestive, carminative and plant-based drinks, which is comparable to the global cereal or vegetable fermentations.

### 2.4 Comparative Analysis of Fermentation Processes

Across these formulations, Sandhana Kalpana orchestrates different microbial ecologies and metabolites: Figure 1

Formulation	Substrate	Microbes	Fermentation Duration	Biotransformations	Therapeutic uses	Reference
Asava	Fresh plant juice/paste	Yeasts ( <i>Saccharomyces</i> spp.), lactic acid bacteria	30-45 days	Glycoside hydrolysis, alcohol production, ester formation	Digestive disorders, immune modulation, general tonic	Samuel et al., 2024
Arishta	Herbal decoction (kwatha)	Yeasts, lactic acid bacteria, acetic acid bacteria	30-45 days	Glycoside hydrolysis, alcohol production, organic acid generation	Respiratory ailments, metabolic disorders, rejuvenation	Samuel et al., 2024
Takra	Fermented buttermilk with herbs	Lactic acid bacteria ( <i>Lactobacillus</i> , <i>Streptococcus</i> spp.)	12-24 hours	Lactose fermentation, protein hydrolysis, herbal extraction	Digestive health, obesity, inflammatory conditions	Mani et al., 2025

Formulation	Substrate	Microbes	Fermentation Duration	Biotransformations	Therapeutic uses	Referene
Kanji	Cereals or vegetables	Lactic acid bacteria (Lactobacillus plantarum, Leuconostoc spp.)	3-7 days	Carbohydrate fermentation, anthocyanin modification, vitamin synthesis	Digestive health, fever, rehydration	Mani et al., 2025

**Figure 1: Comparison of various Sandhana fermentations.**

From the comparative analysis of Sandhana Kalpana (Ayurvedic fermented formulations) we can identify several core features. Firstly, the microbial metabolism is producing organic acids, lactic acid / acetic acid and alcohol is not only helping in extraction of the lipophilic plant constitutions, but it is also acting as a preservative against food spoilage (Mani et al., 2025; Samuel et al., 2024). Second, various microbial enzymes like glycosidases, esterases, proteases break down the complex phytochemical components into simple yet more bio available forms (Mani et al., 2025; Samuel et al., 2024) Third, the fermentation process itself creates new metabolites from both microbes and plants with potentially unique activities (Mani et al., 2025; Samuel et al., 2024; Żółkiewicz et al., 2020).

### 3. Endophytes- the micro-factories of plant cell.

Microorganisms like bacteria and fungi, which primarily inhabits the internal plant tissue like stem, roots, flowers, leaves, seeds for a part of their life cycle without causing visible disease symptoms, these are called endophytes (Maitlo et al., 2025; Perumal et al., 2023). They show symbiotic or common cell relationships and are an integral part of the plant micro ecosystem (Maitlo et al., 2025; Tiwari & Bae, 2022). These endophytes occupy the intracellular spaces or the intercellular spaces and are transmitted horizontally from the environment or vertically via seeds and remain as the endisymbiotic populations (Mousavi & Karami, 2022).

#### 3.1 Roles in medicinal plant health.

Endophytes are omnipresent in vascular plants. Presence of these endophytic communities in medicinal plant is particularly governed by host genotype, organ, age, and environment (Kumari et al., 2023; Pandey et al., 2023). In medicinal plants, presence of endophytes is beneficial in following ways:

- a) Siderophore production, nitrogen fixation, and phytohormone synthesis (auxins, gibberellins) promotes growth and nutrient acquisition in host medicinal plants (Zotchev, 2024; Bankar & Chapadgaonkar, 2025; Mousavi & Karami, 2022).
- b) By modulating, antioxidant system, stress, signalling, and osmotic balance, endosymbionts enhance the tolerance to abiotic stresses, like heavy metals, temperature, salinity, drought etc. (Ogbe et al., 2020; 2019; Upadhyay & Khandelwal, 2025; Pandey et al., 2023).
- c) Through various mechanisms like niche competition, lytic enzymes, induced systemic

resistance and antibiosis endosymbionts increases the resistance of medicinal plant to pathogens and herbivores (Mousavi & Karami, 2022; Tiwari & Bae, 2022).

### 3.2 Endophytes and Secondary Metabolism

Endophytes are abundant producers of secondary metabolites like alkaloids, terpenoids, flavonoids, polyketides, lipopeptides, phenolics, steroids, and tannins along with the anti-inflammatory, anti-cancer, antimicrobial, antioxidant, and immunomodulatory activities (Maitlo et al., 2025; Adeleke & Babalola, 2021; Saini et al., 2025; Mishra et al., 2022; Mousavi & Karami, 2022). All these leads to the fact that endophytes can be treated as the “Microfactories” and microbiomes are the true biosynthetic engine of certain phytochemicals underlining Ayurvedic and other traditional remedies (Kumari et al., 2023; Bankar & Chapadgaonkar, 2025; Pandey et al., 2023).

### 4. Microbial Biotransformation of Phytochemicals

Gut and environmental microbes have the efficacy to alter the pharmacokinetics and pharmacodynamics as they can convert poorly bio available phytochemicals into more absorbable metabolites (Dey, 2019; Kumari et al., 2024) via deglycosylation, dehydroxylation, reduction, and ring-cleavage of polyphenols, terpenoids, and alkaloids, frequently enhancing anti-inflammatory, antioxidant, and anticancer activities (Kumari et al., 2024; Holtz et al., 2024).

### 5. Postbiotics: the magical components of Fermentation

The non-viable, microbial cells, and the short chain, fatty acids, peptides, cell wall fragments, and the exopolysaccharides makes up the postbiotics. Postbiotic are the magic components, produced during the fermentation that shows anti-microbial, immunomodulatory, metabolic and barrier supporting effects (Thorakkattu et al., 2022; Gurunathan et al., 2023) making them better than probiotics.

### 6. Gut Microbiome Modulation and Antimicrobial Resistance

The gut microbiome plays crucial rule in harbouring the resistance gene and acting as a barrier against multi drug resistant pathogens (MDR). Research shows that the nature of diet, probiotics, prebiotics, post biotics, and phytochemicals can effectively influence the gut communities, thereby limiting the MDR colonisation.

### 7. Methodological Toolbox for Microbiome-Mediated Pharmacognosy

During recent times, a wide array of sophisticated techniques enables mechanistic mapping of plant–microbe–host interactions and prediction of microbiome-dependent drug responses. Figure 2.

	Tool	Advantages
1.	Meta-omics (metagenomics, metatranscriptomics,	Identify microbes, pathways, and metabolites involved in drug–microbiome interactions

	metaproteomics, metabolomics)	
2.	Gut fermentation models	Ex vivo prediction of microbial drug/phytochemical transformation
3.	Gnotobiotic/animal models	Causal links between microbes and in vivo pharmacokinetics/dynamics
4.	In silico modeling	Predictive simulations of host–microbe–drug co-metabolism
5.	High-throughput screens	Large-scale interaction maps for drugs and microbiota

**Figure 2: Methodological Toolbox for Microbiome-Mediated Pharmacognosy**

## 8. Research Gaps and Future Directions

Major gaps include: (Figure 3)

Gap	Priority future direction	Citations
Weak causal evidence	Longitudinal, mechanistic, multi-scale pipelines	(Turjeman et al., 2025; Dey, 2019; Bautista et al., 2025)
Non-standardized datasets	Harmonized protocols, shared drug–microbiome databases	(Zhao et al., 2023; Tegegne & Savidge, 2025; Verdegaal & Goodman, 2024)
Poorly characterized postbiotics	Structure–function, dose–response, safety mapping	(Dey, 2019; Mafe & Büsselberg, 2025)
Limited clinical translation	Microbiome-embedded RCTs, AMR and herbal trials	(Gilbert et al., 2025; Bautista et al., 2025; Mafe & Büsselberg, 2025; Verdegaal & Goodman, 2024)
Fragmented analytics	Integrated multi-omics, ML, validated models	(Gronich et al., 2025; Rehman et al., 2025; Kumar et al., 2025)

Figure 3: Main research gaps and aligned future priorities.

## 9. Conclusion

In future, integration of microbiome-mediated pharmacognosy and genetically modified microbiome-based biomarkers and microbiota-derived scaffolds into drug development. The plant-based medicine will get a new direction due to Microbiome-mediated pharmacognosy as a plant–microbe–host system, where desirable therapeutic outcomes could be easily obtained. Incorporating ancient Ayurvedic knowledge into modern day crosscutting technologies will definitely offer more standardised, safer and potentially precision, guided, natural product drug discovery.

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