



RESEARCH ARTICLE

A CRITICAL SYNTHESIS OF COLORECTAL CANCER PATHOGENESIS AND AYURVEDIC CONCEPTUAL FRAMEWORKS: GRAHANI, GULMA, AND ARBUDA PERSPECTIVES

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ABSTRACT

Background: Colorectal cancer (CRC) is a major global health challenge and remains one of the leading causes of cancer-related morbidity and mortality worldwide. According to GLOBOCAN 2022 estimates, approximately 1.93 million new cases and 904,019 deaths were attributed to CRC globally. Contemporary evidence suggests that colorectal carcinogenesis is a multifactorial process involving genetic and epigenetic alterations, chronic inflammation, dietary factors, gut microbiota dysbiosis, and toxin-mediated mutagenesis, including colibactin-induced DNA damage. Although Ayurveda does not describe CRC as a distinct disease entity, several classical concepts, such as *Grahani*, *Gulma*, and *Arbuda*, exhibit significant similarities with different stages of colorectal carcinogenesis. To critically analyse Ayurvedic concepts relevant to colorectal cancer and explore their correlation with contemporary understanding of colorectal carcinogenesis, with particular emphasis on the roles of *Grahani*, *Gulma*, *Arbuda*, *Agni* dysfunction, and *Ama* formation. **Methods:** A critical narrative review was conducted using classical Ayurvedic texts, including Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya, along with contemporary literature retrieved from PubMed, Scopus, and other indexed databases. Relevant studies addressing colorectal cancer pathogenesis, chronic inflammation, gut microbiota, integrative oncology, and Ayurvedic oncology were reviewed and synthesised. Conceptual correlations between Ayurvedic disease constructs and modern biomedical mechanisms were critically evaluated. **Results:** The review identified notable conceptual parallels between Ayurvedic pathophysiology and modern mechanisms of colorectal carcinogenesis. *Grahani*, characterised by Agnimandya and impaired gastrointestinal function, may represent an early functional-inflammatory state associated with chronic intestinal dysfunction and dysbiosis. *Gulma*, described as a localised abdominal mass resulting from Dosha accumulation and *Srotorodha*, may correspond to intermediate stages of localised pathological growth, including adenomatous or premalignant lesions. *Arbuda*, characterised by progressive growth, deep tissue involvement, recurrence, and poor prognosis, demonstrates the closest resemblance to malignant colorectal neoplasia. Furthermore, the Ayurvedic concepts of Agni impairment, Ama accumulation, *Dosha-Dushya Sammurchana*, and chronic inflammation exhibit significant conceptual overlap with contemporary understanding of microbiota-mediated inflammation, epithelial injury, and tumour progression. **Conclusion:** Ayurvedic concepts of *Grahani*, *Gulma*, and *Arbuda* provide a coherent theoretical framework for understanding various stages of colorectal carcinogenesis. Emerging evidence regarding gut microbiota dysbiosis, chronic inflammation, and metabolic dysfunction supports several of these conceptual correlations. Integrating Ayurvedic principles with modern oncological knowledge may offer valuable perspectives for disease prevention, risk stratification, and supportive care in colorectal cancer. Further translational and clinical research is warranted to validate these correlations and explore their potential applications in integrative oncology.

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INTRODUCTION

Colorectal cancer (CRC) is still one of the most dangerous cancers in the world. An estimated 1.93 million new cases and 904,019 fatalities were attributed to it in 2022 alone, and incidence rates in younger populations have been gradually increasing (1). CRC is understood by modern biomedical models as a multistep evolutionary process rather than as an abrupt event. Genetic and epigenetic instability, inflammatory signalling, alteration of the mucosal barrier, microbial

dysbiosis, and environmental risk factors like nutrition and obesity are the main causes of this development (19, 20). The pathophysiology of colorectal cancer has recently placed the gut bacteria at the forefront. While certain bacterial genotoxins, such as colibactin-producing *E. coli*, actively promote malignant transformation and leave enduring mutational signatures, beneficial microbial metabolites, such as short-chain fatty acids, reduce inflammation and dysbiosis (2, 4, 5, 6). Furthermore, a systems-based framework based on the

concepts of Agni (digestive fire), Ama (toxic metabolic byproducts), Dosha (bio-energies), Dhatu (tissues), and Srotas (micro-channels) is provided by Ayurveda. According to this viewpoint, persistent gut problems cause systemic pathology, which eventually structures. Furthermore, Agni (digestive heat), Ama (toxic metabolic wastes), Dosha (bio-energies), Dhatu (tissues), and Srotas (micro-channels) form the foundation of Ayurveda's systems-based architecture. According to this viewpoint, systemic illness resulting from persistent gut dysfunction gradually structuralizes into overt disease (10, 14). Granthi (benign tumors), Arbuda (malignant tumors), precancerous conditions, and chronic inflammation are widely used in the Ayurvedic oncological literature to interpret cancer (11, 12, 13). CRC is a perfect exemplar for this crucial cross-disciplinary synthesis since its etiology is firmly anchored in the gastrointestinal landscape. into overt illness (10, 14). Granthi (benign tumours), Arbuda (malignant tumors), precancerous conditions, and chronic inflammation are all increasingly used in the Ayurvedic oncological literature to interpret cancer (11, 12, 13). CRC is a perfect exemplar for this crucial cross-disciplinary synthesis since its etiology is firmly anchored in the gastrointestinal landscape.

Modern Pathogenesis of Colorectal Cancer: The evolution from normal colonic mucosa to adenomatous change and, ultimately, invasive carcinoma is the foundational explanatory model for sporadic CRC (19). This adenoma–carcinoma sequence is characterised by critical molecular alterations, including APC mutations, mismatch repair deficiency, p53 dysfunction, and profound changes in the tumour microenvironment (20). Inflammation is a well-established driver of this progression. Chronic intestinal inflammation promotes oxidative stress, epithelial damage, aberrant cytokine signalling, and tissue remodelling—all of which foster a pro-tumorigenic environment. The recognised link between inflammatory bowel disease (IBD) and colitis-associated CRC perfectly illustrates how a chronically inflamed terrain precipitates malignancy (3). Furthermore, the microbiome adds a critical layer of complexity. Dysbiosis contributes to CRC via inflammatory signalling, the release of genotoxic compounds, epithelial barrier disruption, and immune evasion (2, 4). Dietary exposures are inextricably linked to this microbial environment; high intakes of red and processed meats, alcohol, and ultra-processed foods elevate CRC risk, whereas plant-forward, high-fibre diets are highly protective (18). These modern nutritional findings closely mirror Ayurvedic principles regarding *Ahara* (diet) and *Viruddhahara* (incompatible food combinations) (7).

Ayurvedic Foundation: Agni, Ama, and the Digestive Terrain: The Ayurvedic framework begins with Agni, the fundamental principle governing digestion, metabolism, and cellular transformation. When Agni is impaired (Agnimandya), incomplete digestion yields Ama—a morbid, obstructive, and toxic substrate characterised by heaviness, stickiness, and a tendency to obstruct physiological channels (Srotorodha) (8). This concept is profoundly relevant to CRC. The gastrointestinal tract is the primary site where metabolic imbalance, dysbiosis, and mucosal barrier dysfunction converge over time. In biomedical terms, this manifests as microbiome-mediated injury and persistent inflammation; in Ayurveda, it is the accumulation of Ama and subsequent Srotorodha (9). While the terminologies differ, the underlying conceptualisation of disease progression is remarkably aligned. Integrative oncology reviews emphasize that Ayurveda's

prevention-oriented tenets—such as Agni support and Rasayana (rejuvenative) therapies—fit seamlessly into a supportive cancer-care model (15, 16, 17).

Grahani: The Early Functional-Inflammatory Stage: Impaired digestive and absorptive function, erratic bowel habits, abdominal discomfort, and chronic gastrointestinal instability classically define *Grahani*. Clinical literature consistently positions *Grahani* as a disorder initiated by deranged Agni and the subsequent systemic spread of Ama (8, 9). From a critical integrative perspective, *Grahani* is the Ayurvedic construct that most accurately corresponds to the early, high-risk terrain of CRC. Both *Grahani* and early pre-neoplastic bowel disease involve persistent intestinal dysfunction, altered bowel habits, mucosal irritation, and microbial disturbance. We propose that *Grahani* represents a functional-to-inflammatory transition state. Repeated dietary indiscretions and weak digestive capacity create a volatile intra-luminal environment, setting the stage for future structural pathology.

Gulma: The Transition Toward Localized Pathology: Ayurvedic texts describe Gulma as a localized, lump-like, or mass-like abdominal disorder, often accompanied by Vata predominance, pain, distension, and obstructive symptoms (10, 11). Due to its diagnostic breadth, Gulma is often viewed as a correlate for various intra-abdominal pathologies, including benign tumors. In the context of CRC, Gulma functions as a conceptual bridge between diffuse functional disease (*Grahani*) and discrete structural lesions (*Arbuda*). Because modern CRC typically begins as a localized adenomatous polyp before becoming invasive, the localized, mass-forming nature of Gulma serves as an elegant Ayurvedic parallel for this intermediate, precancerous stage.

Arbuda: The Classical Analogue to Malignancy: Ayurvedic texts describe Gulma as a localized, lump-like, or mass-like abdominal disorder, often accompanied by Vata predominance, pain, distension, and obstructive symptoms (10, 11). Due to its diagnostic breadth, Gulma is often viewed as a correlate for various intra-abdominal pathologies, including benign tumors. In the context of CRC, Gulma functions as a conceptual bridge between diffuse functional disease (*Grahani*) and discrete structural lesions (*Arbuda*). Because modern CRC typically begins as a localized adenomatous polyp before becoming invasive, the localized, mass-forming nature of Gulma serves as an elegant Ayurvedic parallel for this intermediate, precancerous stage.

Shared Etiological Themes: Diet, Inflammation, and Ecology: The synergy between CRC pathogenesis and Ayurvedic etiology is strongest regarding causative factors: Dietary Risks: Ayurvedic literature links foods such as excessive chilies, heavy curds, and incompatible mixtures to CRC-related states via *Grahani* aggravation (7). This mirrors modern nutritional epidemiology, which indicts low-fiber, high-meat, and ultra-processed diets (18). Microbiota and Inflammation: Modern science details how dysbiosis amplifies inflammation and damages the mucosal barrier (4). Ayurveda captures this exact dynamic through the concept of Ama disrupting the gut environment and localized tissue immunity.

An Integrative, Staged Model of CRC: Synthesising both paradigms yields a highly coherent, staged disease progression model:

Ayurvedic Sequence: *Nidana sevana* (Etiological factors) → *Agnimandya* (Digestive fire impairment) → *Ama* formation (Toxic accumulation) → *Grahani dushti* (Bowel dysfunction) → Chronic inflammation → *Gulma*-like mass formation → *Arbuda*-like malignant transformation.

Biomedical Sequence: Dietary/Lifestyle risk → Microbiome shift → Mucosal inflammation → Adenomatous change → Genetic/Epigenetic instability → Invasive carcinoma. This integrated model is clinically vital. It mandates those chronic digestive disturbances—often dismissed as minor functional complaints—require proactive, preventative intervention before establishing a neoplastic foothold.

Critical Appraisal and Conclusion: The primary strength of this Ayurvedic interpretation is its conceptual coherence. CRC is a disease of chronicity, and Ayurveda excels at explaining disease evolution through functional dysfunction, toxic accumulation, and tissue imbalance. However, a limitation is that this relationship remains inferential; classical texts do not describe histopathological CRC, and not all cases of *Grahani* or *Gulma* progress to cancer.

CONCLUSION

Colorectal cancer (CRC) can be meaningfully interpreted through an Ayurvedic framework by correlating the stages of carcinogenesis with the classical concepts of *Grahani*, *Gulma*, and *Arbuda*. The initial phase of CRC, characterised by chronic intestinal inflammation, dysbiosis, impaired digestion, and mucosal injury, closely resembles *Grahani*, a disorder arising from weakened *Agni* (digestive fire) and the accumulation of *Ama* (toxic metabolic by-products). Persistent digestive dysfunction and doshic imbalance may subsequently progress to *Gulma*, which describes localised abdominal masses and can be conceptually linked to the development of adenomatous polyps, dysplastic lesions, and premalignant growths within the colon. With continued pathological progression, these lesions may evolve into *Arbuda*, a deep-seated, progressively enlarging, and treatment-resistant mass that closely parallels the malignant characteristics of colorectal carcinoma. This Ayurvedic interpretation underscores the importance of maintaining digestive health, metabolic balance, and intestinal integrity as key determinants of disease prevention. Importantly, Ayurveda's emphasis on individualized diet (*Pathya Ahara*), lifestyle regulation (*Dinacharya* and *Ritucharya*), stress management, and early correction of digestive disturbances aligns with contemporary evidence supporting the roles of nutrition, physical activity, and gut microbiota in CRC prevention. Therefore, integrating Ayurvedic preventive and supportive strategies with modern screening methods, molecular diagnostics, surgery, chemotherapy, and targeted therapies may foster a more holistic, proactive, and patient-centered model of colorectal cancer care, focusing not only on disease treatment but also on long-term health promotion, quality of life, and recurrence prevention.

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