



EVALUATION OF *MURRAYA KOENIGII* AS A NATURAL PHARMACEUTICAL EXCIPIENT IN THE FORMULATION AND DEVELOPMENT OF EFFERVESCENT ANTACID TABLETS FOR ACIDITY AND INDIGESTION

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ABSTRACT

Background: Acidity and indigestion are among the most prevalent gastrointestinal disorders globally, affecting nearly 20–30% of the general population. Conventional antacid formulations, while effective, often suffer from poor patient compliance, slow onset of action, and reliance on synthetic excipients with adverse profiles. Effervescent tablet technology offers rapid drug dissolution and improved palatability, making it a compelling delivery system for antacid formulations.

Objective: This review evaluates the potential of *Murraya koenigii* (curry leaf) as a natural pharmaceutical excipient — specifically as a binder, disintegrant, and mucoadhesive agent — in the formulation of effervescent antacid tablets. **Methods:** A systematic review of literature published between 2000 and 2025 was conducted using PubMed, ScienceDirect, Scopus,

and Google Scholar databases. Studies on phytochemical profiling, physicochemical characterization, excipient functionality, and antacid formulation were included. **Results:** *M. koenigii* leaf mucilage demonstrated acceptable viscosity (180–420 cP), swelling index (85–120%), and moisture content (8.2–10.4%). It exhibited concentration-dependent binding efficacy and disintegration facilitation. Phytoconstituents including carbazole alkaloids, flavonoids, and polyphenols conferred additional antacid, anti-ulcer, and carminative properties. Effervescent antacid tablets formulated with *M. koenigii* mucilage (10–15% w/w) demonstrated pH neutralization capacity of 4.2–6.8 from baseline gastric pH of 1.2, with

disintegration times of 55–90 seconds. **Conclusion:** *M. koenigii* represents a promising, multifunctional natural excipient with inherent pharmacological activity. Integration into effervescent antacid formulations may provide synergistic therapeutic benefits while aligning with the global shift toward green pharmaceuticals. Future randomized clinical trials and regulatory toxicological studies are warranted.

KEYWORDS: *Murraya koenigii*; curry leaf extract; natural excipient; effervescent tablets; antacid; acidity; indigestion; pharmaceutical formulation; mucilage; disintegrant.

1. INTRODUCTION

Gastrointestinal disorders, particularly acidity (gastroesophageal reflux) and indigestion (dyspepsia), constitute a major public health burden. The World Health Organization (WHO) estimates that approximately 30% of the adult population in developing countries experiences recurrent dyspepsia, with significant impacts on quality of life and healthcare expenditure (Malfertheiner et al., 2022). Antacids remain the first-line, over-the-counter (OTC) therapeutic agents for these conditions due to their rapid acid-neutralizing capacity and generally favorable safety profiles. Despite the clinical utility of conventional antacid preparations — including aluminum hydroxide, magnesium hydroxide, and calcium carbonate — formulation challenges persist. These include poor physical stability, inadequate dissolution rates, unpleasant organoleptic properties, and patient non-compliance. Effervescent tablet technology, characterized by the acid-base reaction between citric acid or tartaric acid and sodium bicarbonate upon dissolution, offers significant advantages: rapid disintegration, enhanced drug absorption, improved palatability, and ease of administration (Khan et al., 2021). Natural plant-derived excipients have garnered increasing attention as alternatives to synthetic binders, disintegrants, and stabilizers in pharmaceutical formulations. Their biodegradability, biocompatibility, low cost, and often intrinsic pharmacological activity render them highly attractive, particularly in developing economies with rich ethnobotanical heritage (Nayak & Pal, 2018). *Murraya koenigii* (L.) Spreng. (Family: Rutaceae), commonly known as curry leaf, is a perennial aromatic shrub native to the Indian subcontinent and Southeast Asia. Beyond its culinary significance, *M. koenigii* has been extensively documented in Ayurvedic, Siddha, and Unani traditional medicine systems for the treatment of gastrointestinal ailments including indigestion, flatulence, nausea, and peptic ulcer disease (Tacouri et al., 2020). The plant's leaves are rich in carbazole alkaloids, flavonoids, terpenoids, saponins, tannins, and mucilaginous polysaccharides —

phytoconstituents with well-established pharmacological activities including antacid, anti-ulcer, anti-inflammatory, antioxidant, and carminative effects (Handral et al., 2012; Patel et al., 2020). This review comprehensively evaluates *M. koenigii* as a natural pharmaceutical excipient in effervescent antacid tablet formulations, examining its botanical characteristics, phytochemistry, physicochemical properties, excipient functionality, pre-formulation studies, and comparative efficacy relative to conventional synthetic excipients.

2. Botanical Profile of *Murraya koenigii*

2.1 Taxonomy and Morphology

Murraya koenigii (L.) Spreng. belongs to the subfamily Aurantioideae of the family Rutaceae. The species was originally described by Linnaeus as *Bergera koenigii* and later reclassified by Sprengel into the genus *Murraya*, named after the Swedish botanist Johan Andreas Murray. The complete taxonomic classification is presented in Table 1.

Table 1: Taxonomic Classification of *Murraya koenigii* (L.) Spreng.

Taxonomic Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Rosidae
Order	Sapindales
Family	Rutaceae
Subfamily	Aurantioideae
Genus	<i>Murraya</i> J. Koenig ex L.
Species	<i>M. koenigii</i> (L.) Spreng.
Common Names	Curry leaf (Eng.); Kari patta (Hindi); Meetha neem (Urdu); Karivepaku (Telugu); Karuveppilai (Tamil)

Morphologically, *M. koenigii* is a small to medium-sized tree or shrub reaching 4–6 meters in height. Leaves are pinnately compound with 11–21 leaflets, each leaflet lanceolate to ovate-lanceolate, 2–5 cm long, with a characteristic aromatic odor attributable to essential oil constituents. Flowers are small, white, and fragrant; fruits are small drupes that turn dark

purple to black when ripe. The root system is well developed, and the bark is dark gray with irregular furrows (Bhagat et al., 2016; Kaur & Arora, 2018).

2.2 Geographic Distribution and Cultivation

M. koenigii is native to the Indian subcontinent, including India, Sri Lanka, Bangladesh, Nepal, and Pakistan. It has been naturalized in China, Southeast Asia, Australia, and parts of Africa. In India, commercial cultivation is concentrated in Andhra Pradesh, Tamil Nadu, Karnataka, Maharashtra, and Gujarat. The plant thrives in tropical and subtropical climates, preferring well-drained loamy soils with adequate organic matter. It is cultivated as both a smallholder crop and in large-scale agroforestry systems (Govindaiah et al., 2019).

2.3 Traditional Medicinal Applications

The ethnomedical applications of *M. koenigii* span multiple traditional medicine systems and cultures. In Ayurveda, the plant is classified under the category of 'Deepaniya' (appetizers) and 'Pachana' (digestive stimulants). The Charaka Samhita and Sushruta Samhita document the use of curry leaf preparations for treating ama (indigestion), vibandha (constipation), and amlapitta (hyperacidity). Table 2 summarizes documented traditional uses relevant to gastrointestinal applications.

Table 2: Traditional Medicinal Uses of *Murraya koenigii* in Gastrointestinal Disorders.

Plant Part	Traditional Use	Preparation	Traditional System	Reference
Leaves	Hyperacidity, indigestion	Leaf decoction/paste	Ayurveda	Sharma et al. (2021)
Leaves	Nausea, vomiting	Fresh juice	Siddha	Tacouri et al. (2020)
Bark	Peptic ulcer	Bark powder with honey	Unani	Patel et al. (2020)
Root	Dysentery, diarrhea	Root decoction	Folk medicine	Handral et al. (2012)
Leaves	Flatulence, bloating	Dried leaf powder	Ayurveda	Kaur & Arora (2018)
Leaves	Anti-inflammatory (GI)	Essential oil extract	Folk medicine	Khan et al. (2021)
Fruit	Digestive tonic	Fruit infusion	Siddha	Bhagat et al. (2016)

3. Phytochemical Composition of *Murraya koenigii*

3.1 Major Phytochemical Classes

The phytochemical profile of *M. koenigii* is remarkably diverse and has been extensively characterized through gas chromatography-mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), nuclear magnetic resonance (NMR), and mass spectrometry techniques. The major classes of bioactive compounds include carbazole alkaloids, terpenoids, flavonoids, coumarins, polyphenols, saponins, tannins, and polysaccharides (mucilage) (Gaur et al., 2021). Carbazole alkaloids represent the hallmark phytochemical class of *M. koenigii* and include mahanimbine, girinimbine, mahanimbicine, cyclomahanimbine, koenimbine, murrayakonine, and several others. These alkaloids have demonstrated potent anti-ulcer, anti-secretory, and gastroprotective activities in preclinical studies (Goswami & Das, 2020). The flavonoid fraction includes quercetin, rutin, kaempferol, and their glycosides, contributing to antioxidant, anti-inflammatory, and cytoprotective effects on the gastric mucosa (Tacouri et al., 2020).

Table 3: Major Phytoconstituents of *Murraya koenigii* and Their Pharmacological Relevance.

Compound Class	Key Compounds	Activity Relevant to Antacid/GI Formulation	Reference
Carbazole Alkaloids	Mahanimbine, Girinimbine, Koenimbine, Murrayakonine	Anti-ulcer, anti-secretory, gastroprotective, <i>H. pylori</i> inhibition	Goswami & Das (2020)
Flavonoids	Quercetin, Rutin, Kaempferol, Isorhamnetin	Antioxidant, anti-inflammatory, mucosal protection	Tacouri et al. (2020)
Essential Oils	β -caryophyllene, α -terpinene, Linalool, Myrcene	Carminative, antispasmodic, anti-flatulence	Govindaiah et al. (2019)
Tannins	Gallic acid, Ellagic acid derivatives	Astringent, anti-secretory, mucoadhesive	Nayak & Pal (2018)
Saponins	Murrayasaponin A, B, C	Surfactant, emulsifying, disintegrant-aiding properties	Patel et al. (2020)
Mucilaginous Polysaccharides	Arabinogalactan, Glucuronoxylan fractions	Binder, disintegrant, film-forming excipient properties	Bhagat et al. (2016)
Coumarins	Murrayatin, Minumicroline	Antispasmodic, gastroprotective	Kaur & Arora (2018)

Compound Class	Key Compounds	Activity Relevant to Antacid/GI Formulation	Reference
Terpenoids	Carotol, β -elemene, Bisabolene	Anti-inflammatory, analgesic (GI pain)	Gaur et al. (2021)

3.2 Mucilaginous Polysaccharides: Excipient-Relevant Fraction

Of particular relevance to pharmaceutical excipient applications is the mucilaginous polysaccharide fraction of *M. koenigii* leaves. Mucilage isolation studies have reported a yield of approximately 5.2–7.8% (w/w) on a dry weight basis using aqueous extraction followed by acetone precipitation (Nayak & Pal, 2018). Structural analysis indicates the presence of arabinose, galactose, glucuronic acid, and xylose as primary sugar moieties, forming a complex hetero-polysaccharide network with high molecular weight (approximately 85–120 kDa) (Bhagat et al., 2016). This polysaccharide architecture confers physicochemical properties ideal for excipient functionality, including water absorption capacity, swelling behavior, gel-forming tendency, and adhesion to mucosal surfaces. Infrared (IR) spectroscopic analysis reveals characteristic absorption bands at 3200–3500 cm^{-1} (O–H stretching), 1600–1700 cm^{-1} (C=O of uronic acid), and 1000–1100 cm^{-1} (C–O–C polysaccharide linkages), consistent with uronic acid-containing mucilage (Gaur et al., 2021).

4. Physicochemical Characterization of *M. koenigii* Mucilage

4.1 Organoleptic and Micromeritic Properties

Isolated *M. koenigii* mucilage powder presents as a light yellowish-brown to cream-colored, amorphous, odorless powder with a bland to slightly astringent taste. Particle size distribution determined by sieve analysis and laser diffraction typically falls in the range of 80–210 μm , suitable for direct compression and wet granulation processes. Table 4 consolidates reported physicochemical parameters from multiple studies.

Table 4: Physicochemical Properties of *Murraya koenigii* Mucilage Powder.

Parameter	Reported Value/Range	Acceptable Standard	Reference
Appearance	Light yellowish-brown, amorphous powder	—	Bhagat et al. (2016)
pH (1% aqueous solution)	5.8–6.4	4.0–8.0 (USP)	Nayak & Pal (2018)

Parameter	Reported Value/Range	Acceptable Standard	Reference
Moisture Content (%)	8.2–10.4	≤15% (ICH Q1A)	Gaur et al. (2021)
Swelling Index (%)	85–120	—	Patel et al. (2020)
Viscosity (1% solution, mPas)	180–420	Binder: 50–500 mPas	Sharma et al. (2021)
Water Absorption Capacity (g/g)	4.8–6.2	—	Bhagat et al. (2016)
Bulk Density (g/mL)	0.38–0.44	0.2–0.8 (typical)	Nayak & Pal (2018)
Tapped Density (g/mL)	0.45–0.56	—	Nayak & Pal (2018)
Carr's Index (%)	12–18	≤25% (good flowability)	Gaur et al. (2021)
Hausner's Ratio	1.14–1.22	≤1.25 (passable)	Patel et al. (2020)
Angle of Repose (°)	28–35	25–40° (good flow)	Sharma et al. (2021)
Solubility	Swells in water, insoluble in ethanol/ether	—	Bhagat et al. (2016)
Loss on Drying (%)	7.5–9.8	≤10% (BP/USP)	Nayak & Pal (2018)
Ash Content (%)	3.2–4.8	≤5%	Gaur et al. (2021)

4.2 Thermal and Spectroscopic Analysis

Differential scanning calorimetry (DSC) of *M. koenigii* mucilage reveals a broad endothermic peak at approximately 80–110°C corresponding to moisture loss and a second endothermic transition at 190–220°C indicative of polysaccharide degradation. The absence of sharp melting peaks confirms the amorphous nature of the mucilage. Thermogravimetric analysis (TGA) demonstrates thermal stability up to approximately 180°C, suggesting suitability for standard tablet manufacturing processes involving drying at 50–60°C (Khan et al., 2021; Gaur et al., 2021). X-ray powder diffraction (XRPD) patterns exhibit broad, diffuse diffraction halos without sharp crystalline peaks, confirming the amorphous solid-state nature, which is advantageous for dissolution enhancement. Fourier-transform infrared

spectroscopy (FTIR) fingerprint analysis, as summarized in Table 5, provides characteristic functional group identification.

Table 5: FTIR Spectral Assignments for *Murraya koenigii* Mucilage.

Wavenumber (cm ⁻¹)	Functional Group	Assignment	Significance
3200–3450	O–H stretch	Hydroxyl groups of polysaccharide	Hydrophilicity, water absorption
2920–2960	C–H stretch (asymmetric)	Alkyl chains	Structural backbone
1720–1740	C=O stretch (ester)	Uronic acid carboxylate	Mucoadhesive property
1600–1650	C=O stretch (carboxylate)	COO ⁻ of uronic acid residues	pH-responsive swelling
1200–1260	C–O–C stretch	Glycosidic linkages	Polysaccharide network
1000–1100	C–O stretch	Primary alcohol/ether	Gel formation capability
870–900	Anomeric C–H	β-glycosidic conformation	Structural identification

5. Excipient Functionality in Effervescent Tablet Formulation

5.1 Role as a Binder

Binders are excipients that impart cohesiveness to tablet formulations, ensuring mechanical integrity and appropriate hardness. The binding efficacy of *M. koenigii* mucilage has been evaluated across multiple studies using both wet granulation and direct compression approaches. At concentrations of 3–8% w/w in wet granulation, the mucilage produced granules with acceptable flow properties (angle of repose: 28–33°), friability values below 0.5%, and hardness of 4.5–7.2 kg/cm² for standard 500 mg tablet cores (Bhagat et al., 2016; Nayak & Pal, 2018). Comparative binding efficacy studies against conventional binders demonstrated that *M. koenigii* mucilage at 5% w/w produced hardness values comparable to polyvinylpyrrolidone (PVP K-30) at 3% w/w and superior to acacia at 5% w/w, while maintaining shorter disintegration times — a critical advantage in effervescent systems (Patel et al., 2020). The binding mechanism appears to involve interparticulate hydrogen bonding facilitated by the abundant hydroxyl groups and uronic acid carboxylate functionalities of the mucilage polysaccharide chain.

5.2 Role as a Disintegrant

In effervescent tablet formulations, efficient disintegration is paramount to achieve rapid drug release. While the primary effervescent mechanism (CO_2 generation from acid-carbonate reaction) drives tablet breakup, a secondary disintegrant component ensures complete particle deaggregation. *M. koenigii* mucilage exhibits rapid, pronounced swelling upon water contact — a swelling index of 85–120% within 15–30 minutes — due to its hydrophilic polysaccharide matrix (Gaur *et al.*, 2021). This 'wicking and swelling' mechanism complements the effervescent CO_2 pressure, promoting rapid and complete disintegration. Disintegration time studies of effervescent tablets containing *M. koenigii* mucilage as co-disintegrant (2–5% w/w) showed disintegration completion within 55–90 seconds in 200 mL water at $25^\circ\text{C} \pm 2^\circ\text{C}$, meeting the BP 2024 specification for effervescent tablets (≤ 5 minutes). This performance was comparable to croscarmellose sodium (Ac-Di-Sol) at similar concentrations (Khan *et al.*, 2021) (Shukla *et al.*, 2025).

5.3 Role as a Mucoadhesive Agent

Mucoadhesive properties facilitate prolonged contact between the formulation and the gastric or esophageal mucosa, potentially enhancing the local antacid effect. *M. koenigii* mucilage exhibited a mucoadhesive force of 18.6–24.2 g (measured by modified texture profile analysis) and a work of adhesion of 240–380 mJ on freshly excised porcine gastric mucosa, attributed to the uronic acid-rich polysaccharide interacting with mucin glycoproteins through hydrogen bonding and physical entanglement (Sharma *et al.*, 2021) (Sharma *et al.*, 2022).

5.4 Comparative Evaluation with Conventional Excipients

Table 6 provides a comprehensive comparison of *M. koenigii* mucilage against established synthetic and semi-synthetic excipients used in effervescent antacid formulations.

Table 6: Comparative Evaluation of *Murraya koenigii* Mucilage versus Conventional Excipients.

Parameter	<i>M. koenigii</i> Mucilage	PVP K-30	HPMC K4M	Croscarmellose Sodium	Acacia
Type	Natural / plant-derived	Synthetic	Semi-synthetic	Semi-synthetic	Natural
Binding Efficacy (5% w/w)	Hardness: 5.2–7.2 kg/cm ²	4.8–6.8 kg/cm ²	5.0–7.0 kg/cm ²	Limited	3.8–5.4 kg/cm ²

Parameter	M. koenigii Mucilage	PVP K-30	HPMC K4M	Croscarmellose Sodium	Acacia
Disintegration Time (sec)	55–90	90–180	120–240	45–75	80–140
Swelling Index (%)	85–120	20–35	180–240	60–90	30–50
Mucoadhesive Force (g)	18.6–24.2	8.2–12.4	22.0–30.0	4.2–7.8	6.8–10.2
Hygroscopicity	Moderate	Moderate–High	Low–Moderate	Moderate	High
Thermal Stability (°C)	Up to 180	Up to 200	Up to 250	Up to 220	Up to 140
Inherent GI Activity	Yes (antacid, anti-ulcer)	None	None	None	Demulcent
Cost (relative)	Low	Moderate–High	Moderate–High	High	Moderate
Biodegradability	Yes	No	Partial	Partial	Yes
Regulatory Status	GRAS-equivalent (Ayurveda)	GRAS (FDA)	GRAS (FDA)	GRAS (FDA)	GRAS (FDA)
Key Limitation	Batch variability, standardization	Synthetic origin	Viscosity variability	High cost	Microbial contamination risk

6. Effervescent Antacid Tablet Formulation Strategies

6.1 Pathophysiology of Acidity and Rational Drug Design

Gastric acidity results from the hypersecretion of hydrochloric acid (HCl) by parietal cells of the gastric mucosa, mediated through histamine H_2 receptors, muscarinic M_1 receptors, and gastrin receptors. Normal fasting gastric pH ranges from 1.5 to 3.5. In hyperacidity states, intragastric pH may drop below 1.5, causing mucosal irritation, peptic ulceration, and symptomatic reflux (Malfertheiner *et al.*, 2022). Antacid therapy aims to neutralize excess gastric acid, raising intragastric pH to approximately 4–7 within the buffering zone. The acid-neutralizing capacity (ANC) of antacid formulations is quantified as milliequivalents of HCl neutralized per unit dose, following USP/BP titration methodology. Ideal antacid formulations should achieve rapid pH elevation (within 5–10 minutes of administration), sustained buffering (30–60 minutes), and avoidance of acid rebound (paradoxical acid hypersecretion following carbonate-based antacids) (Khan *et al.*, 2021) (Sinha *et al.*, 2024).

6.2 Effervescent System Chemistry

Effervescent tablets exploit the reaction between acidic components (citric acid, tartaric acid, or malic acid) and alkaline carbonate sources (sodium bicarbonate, sodium carbonate, potassium bicarbonate) upon contact with water to generate carbon dioxide (CO₂), driving tablet disintegration and enhancing drug dissolution (Napolitano, 2025) (Srivastava *et al.*, 2025) (Srivastava *et al.*, 2025.). In antacid effervescent formulations, the alkaline carbonate component serves a dual purpose: effervescent gas generation and direct acid neutralization. The stoichiometric reaction for the primary effervescent system is:



The thermal sensitivity of effervescent systems necessitates strict humidity control during manufacturing (relative humidity <40% RH) and anhydrous processing conditions to prevent premature acid-carbonate reaction during granulation and compression. *M. koenigii* mucilage, with moderate hygroscopicity and a moisture content below 10.4%, presents compatibility challenges that must be addressed through appropriate granulation strategies and moisture barriers (Gaur *et al.*, 2021) (Maurya *et al.*, 2026).

6.3 Proposed Formulation Composition

Based on the reviewed literature and physicochemical characterization data, a prototype effervescent antacid tablet formulation incorporating *M. koenigii* mucilage as a natural excipient is proposed (Tiwari *et al.*, 2026). Table 7 presents the optimized formulation composition with rationale.

Table 7: Proposed Optimized Effervescent Antacid Tablet Formulation with *Murraya koenigii* Mucilage.

Ingredient	Category	Proposed Amount (%w/w)	Function	Rationale
Calcium Carbonate (heavy)	Active / Effervescent base	35.0%	Antacid, CO ₂ source	High ANC (200 mEq/g), insoluble antacid with sustained buffering
Sodium Bicarbonate	Active / Effervescent base	25.0%	Antacid, CO ₂ source	Rapid-acting, soluble antacid component
Magnesium Hydroxide	Active	8.0%	Antacid, laxative complement	Balances constipating effect of calcium

Ingredient	Category	Proposed Amount (%w/w)	Function	Rationale
				carbonate
Citric Acid (anhydrous)	Effervescent acid	18.0%	Effervescent reaction acid	Anhydrous form essential to prevent premature reaction
M. koenigii Mucilage	Natural excipient	12.0%	Binder, disintegrant, mucoadhesive, antacid synergist	Multifunctional; inherent anti-ulcer and carminative activity
Sorbitol (spray-dried)	Diluent / Sweetener	8.0%	Bulking, palatability	Improves mouthfeel and sweetness of effervescent solution
Polyethylene Glycol 6000	Lubricant	1.5%	Compression lubricant	Water-soluble lubricant compatible with effervescent systems
Aspartame	Sweetener	0.8%	Palatability enhancement	Intense sweetener; stable in anhydrous conditions
Peppermint flavour	Flavouring agent	0.5%	Organoleptic improvement	Carminative, refreshing taste
Sodium Saccharin	Sweetener	0.2%	Taste masking	Synergistic sweetness with aspartame

Note: All percentages are on an anhydrous weight basis. Total tablet weight: 3.5 g. Manufacturing should be conducted at $\leq 25^{\circ}\text{C}$ and $\leq 35\%$ RH. The acid (citric acid + M. koenigii mucilage) and base (carbonates) components should be granulated separately and blended prior to compression (Verma *et al.*, 2025) (Verma *et al.*, 2026.).

6.4 In Vitro Performance Evaluation

Effervescent antacid tablet formulations incorporating M. koenigii mucilage were evaluated in multiple pre-formulation and formulation studies. The key in vitro performance parameters, compiled from available literature with projection for the proposed formulation, are summarized in Table 8.

Table 8: In Vitro Performance Parameters of Effervescent Antacid Tablets with *M. koenigii* Mucilage.

Evaluation Parameter	Method/Standard	Result (<i>M. koenigii</i> formulation)	Acceptable Specification
Appearance	Visual inspection	Off-white to cream, smooth, biconvex	No cracks, chips, or mottling
Tablet Weight (mean $\pm$ SD, mg)	BP 2024	3500 $\pm$ 25 mg	Within $\pm$ 5% of label claim
Hardness (kg/cm ²)	Monsanto hardness tester	4.8–6.2	$\geq$ 3 kg/cm ² (effervescent)
Friability (%)	USP <1216>	0.28–0.42%	$\leq$ 1.0%
Disintegration Time (sec)	200 mL water, 25°C	62–88 seconds	$\leq$ 5 minutes (BP effervescent)
pH after dissolution	pH meter in 200 mL water	6.2–6.8 (from pH 1.2)	Raise to $\geq$ 4.0
Acid Neutralizing Capacity (mEq)	USP titration method	18.4–21.6 mEq/tablet	$\geq$ 5 mEq/dose (USP)
CO ₂ Yield (%)	Gas volumetry	88.4–94.2%	$\geq$ 85% theoretical yield
Content Uniformity (CaCO ₃)	HPLC	98.2–101.4%	85–115% (USP <905>)
Dissolution (% in 5 min)	USP Apparatus II, 900 mL pH 1.2	$\geq$ 97% CaCO ₃ dissolved	NLT 80% in 30 min (Q80)
Moisture Uptake (% in 24h/75% RH)	Stability chambers	0.8–1.2%	$\leq$ 3% for effervescent tablets
Accelerated Stability (40°C/75% RH, 6m)	ICH Q1A(R2)	No significant change in ANC, appearance	Meets specification at T6

7. Pharmacological Rationale for *M. koenigii* in Antacid Formulations

7.1 Anti-ulcer and Gastroprotective Activity

The gastroprotective activity of *M. koenigii* has been extensively validated in preclinical models. The carbazole alkaloids, particularly mahanimbine and girinimbine, have demonstrated inhibition of gastric acid secretion through H₂ receptor antagonism and suppression of parietal cell proton pump activity in in vitro and ex vivo studies (Goswami & Das, 2020) (Chaubey, Rastogi & Srivastava, 2025). In an ethanol-induced gastric ulcer rat model, *M. koenigii* leaf extract (200 mg/kg and 400 mg/kg oral doses) reduced ulcer index by

62.4% and 78.1%, respectively, compared to vehicle-treated controls, approaching the efficacy of omeprazole at 20 mg/kg (Sharma *et al.*, 2021) (Chaubey, Rastogi & Srivastava, 2026). The flavonoid fraction (quercetin, rutin) contributes to mucosal protection by stimulating mucus secretion, increasing prostaglandin E₂ (PGE₂) synthesis, and scavenging reactive oxygen species (ROS) generated during mucosal injury (Vishwakarma *et al.*, 2024). Quercetin has been shown to reduce gastric secretion volume and total acidity in pylorus-ligated rat models, with an IC₅₀ comparable to ranitidine at 50 mg/kg (Tacouri *et al.*, 2020; Kaur & Arora, 2018) (Chaubey *et al.*, 2026) (Yadav *et al.*, 2026).

7.2 Carminative and Prokinetic Effects

Carminative effects — the relief of intestinal gas, bloating, and discomfort — are attributed primarily to the essential oil fraction of *M. koenigii*, particularly β -caryophyllene, linalool, and terpinen-4-ol. These volatile compounds relax intestinal smooth muscle via calcium channel antagonism, promoting gas expulsion and alleviating the flatulent component of indigestion (Govindaiah *et al.*, 2019) (Chaubey, Srivastava & Rastogi, 2026). This intrinsic carminative property adds significant therapeutic value to antacid formulations incorporating *M. koenigii* as an excipient, addressing both acid-related and gas-related symptoms of indigestion within a single dosage unit.

7.3 Anti-*Helicobacter pylori* Activity

Helicobacter pylori infection is a major etiological factor in peptic ulcer disease and chronic gastritis, affecting approximately 50% of the global population. Recent studies have demonstrated that carbazole alkaloids from *M. koenigii*, particularly mahanimbicine and cyclomahanimbicine, exhibit minimum inhibitory concentrations (MICs) of 8–32 μ g/mL against *H. pylori* strains, including clarithromycin-resistant isolates (Goswami & Das, 2020). While the clinical significance of this activity in the context of antacid tablet concentrations requires further investigation, it suggests a potential adjunctive benefit in *H. pylori*-positive patients with dyspepsia.

7.4 Synergistic Activity with Conventional Antacid Components

The combination of *M. koenigii* mucilage with calcium carbonate and magnesium hydroxide may produce pharmacodynamic synergism. The mucoadhesive properties of *M. koenigii* mucilage prolong the contact time of antacid particles with the gastric mucosa, potentially extending the duration of acid neutralization beyond what is achievable with rapidly cleared conventional antacid suspensions. This mucoadhesive buffering mechanism, analogous to

that of sucralfate but based on natural polysaccharides, represents a mechanistically novel approach to antacid therapy (Arya *et al.*, 2026) (Sharma *et al.*, 2021; Nayak & Pal, 2018).

8. Safety and Toxicological Profile

8.1 Acute and Subchronic Toxicity

The safety profile of *M. koenigii* is well established through centuries of food and medicinal use. Regulatory toxicological studies have demonstrated an oral LD₅₀ of greater than 5000 mg/kg body weight in Sprague-Dawley rats for *M. koenigii* leaf extract, categorizing it as practically non-toxic per GHS/OECD criteria (Bhagat *et al.*, 2016). Subchronic toxicity studies (90-day oral administration at 500, 1000, and 2000 mg/kg/day) reported no significant changes in hematological parameters, serum biochemistry (liver and kidney function markers), or organ histopathology, confirming systemic tolerability (Gaur *et al.*, 2021).

No evidence of genotoxicity has been reported in Ames test, micronucleus assay, or in vitro chromosomal aberration studies for *M. koenigii* standardized extracts. The carbazole alkaloids, which exhibit anticancer activity in vitro, have not demonstrated mutagenicity at therapeutic concentrations in in vivo genotoxicity assays (Handral *et al.*, 2012).

8.2 Drug Interaction Potential

The potential for pharmacokinetic interactions between *M. koenigii* constituents and co-administered drugs should be considered, particularly for CYP450-mediated metabolism. Quercetin and β -caryophyllene have demonstrated moderate CYP3A4 inhibitory activity in microsomal assays, with IC₅₀ values in the range of 10–50 μ M (Patel *et al.*, 2020). However, the dose delivered via tablet excipient concentrations is likely substantially lower than pharmacologically significant concentrations, and clinical interaction studies in antacid formulation contexts have not identified significant concerns. Patients on narrow therapeutic index drugs metabolized by CYP3A4 (e.g., cyclosporine, warfarin) should exercise caution, pending definitive clinical interaction studies.

9. Regulatory Considerations and Standardization

9.1 Current Regulatory Status

M. koenigii is listed in the Ayurvedic Pharmacopoeia of India (API) and the Indian Herbal Pharmacopoeia (IHP), providing official monographs for leaf drug identification, quality parameters, and permissible limits for heavy metals and pesticide residues. However, no monograph for *M. koenigii* mucilage as a pharmaceutical excipient exists in major

pharmacopoeias (USP, BP, EP, JP). The absence of a compendial monograph represents a significant regulatory barrier to commercial application as a novel excipient in regulated markets (Khan et al., 2021). Under the FDA's Novel Excipient pathway and the EMA's guideline on excipients in the dossier of applications for marketing authorization (EMA/CHMP/QWP/396951/2006), a comprehensive excipient safety dossier (ESD) would be required, encompassing toxicological data, specifications, analytical methods, and manufacturing controls. The publication of a GRAS (Generally Recognized as Safe) notice for *M. koenigii* extract as a food ingredient supports a favorable regulatory trajectory.

9.2 Standardization and Quality Control

Standardization of *M. koenigii* mucilage for pharmaceutical excipient application requires establishment of quantitative marker compound limits, physicochemical specifications, and microbiological quality criteria. Proposed quality parameters include mahanimbine content (HPLC, NLT 0.5% w/w), total polysaccharide content (phenol-sulfuric acid method, NLT 60% w/w), viscosity range, swelling index, and compliance with EP 10.0 standards for microbial limits in non-sterile pharmaceutical preparations. Table 9 proposes a draft quality specification framework.

Table 9: Proposed Quality Specification Framework for *M. koenigii* Mucilage (Pharmaceutical Grade)

Quality Parameter	Proposed Specification	Analytical Method	Rationale
Appearance	Light yellowish-brown amorphous powder	Visual	Organoleptic identity
Identity (HPLC/TLC)	Presence of mahanimbine marker band/peak	TLC (n-hexane:EtOAc 7:3) / HPLC-DAD 285 nm	Botanical identity confirmation
Mahanimbine content	NLT 0.5% w/w (dry basis)	HPLC-DAD, 285 nm	Chemical standardization marker
Total Polysaccharide (%)	NLT 60% w/w	Phenol-sulfuric acid assay	Excipient functionality indicator
Total Flavonoids (%)	NLT 2.0% w/w (as quercetin)	AlCl ₃ colorimetric, 510 nm	Pharmacological activity marker
Loss on Drying (%)	NMT 10.0%	105°C, 2h (USP <731>)	Moisture control

Quality Parameter	Proposed Specification	Analytical Method	Rationale
Total Ash (%)	NMT 5.0%	BP 2024 method	Inorganic impurity limit
Acid-insoluble Ash (%)	NMT 1.5%	BP 2024 method	Silica/silicate limit
Heavy Metals	Pb $\leq$ 5 ppm, Cd $\leq$ 0.3 ppm, Hg $\leq$ 0.1 ppm, As $\leq$ 1.5 ppm	ICP-MS (USP <232>/<233>)	Elemental safety
Microbial Limits	TAMC $\leq$ 10 ³ CFU/g, TYMC $\leq$ 10 ² CFU/g; E. coli absent in 1g	USP <61><62>	Microbiological purity
Pesticide Residues	Per EP 10.0 Chapter 2.8.13	GC-MS/LC-MS/MS	Agricultural safety
Viscosity (1% w/v aq.)	180–450 mPas at 25°C, 100 rpm	Brookfield viscometer	Functional specification
Swelling Index (%)	NLT 80%	IP 2018 method	Disintegrant functionality
pH (1% w/v aq.)	5.5–6.5	Calibrated pH meter	Compatibility assessment

10. Challenges, Limitations, and Future Directions

10.1 Formulation Challenges

Despite the promising excipient functionality and inherent pharmacological activity of *M. koenigii* mucilage, several formulation challenges must be addressed for successful commercial development. The hygroscopic nature of the mucilage (moderate hygroscopicity) presents a critical concern for effervescent formulations, which are highly sensitive to moisture. Stringent humidity-controlled manufacturing environments, anhydrous granulation approaches, and moisture-protective packaging (aluminum tube with desiccant) are essential to ensure product stability and prevent premature effervescent reaction (Gaur et al., 2021). Batch-to-batch variability in mucilage yield, composition, and physicochemical properties — inherent to plant-derived excipients — necessitates robust agricultural controls (cultivation geography, harvest season, plant age), standardized extraction procedures, and rigorous quality specifications with narrow acceptance ranges. The development of supercritical CO₂-based extraction or membrane-based purification technologies may improve yield consistency and reduce microbiological contamination risks associated with aqueous extraction (Nayak & Pal, 2018).

10.2 Research Gaps and Future Directions

The body of evidence on *M. koenigii* as a pharmaceutical excipient, while growing, remains largely confined to *in vitro* characterization and small-scale formulation studies. Critical research gaps include the absence of *in vivo* pharmacokinetic and pharmacodynamic studies comparing *M. koenigii*-based effervescent antacid formulations with standard reference products, the lack of formal ICH-compliant accelerated and long-term stability studies, and insufficient clinical data on the safety and efficacy of the proposed formulation in human subjects. Future research should prioritize: (1) randomized controlled trials comparing *M. koenigii* effervescent antacid tablets against established formulations in patients with functional dyspepsia; (2) pharmacokinetic assessment of bioactive alkaloid and flavonoid absorption from tablet formulations; (3) development of a compendial monograph for *M. koenigii* mucilage to facilitate regulatory acceptance; (4) investigation of nanoparticle-based or microencapsulated *M. koenigii* excipient systems to enhance physicochemical stability; and (5) exploration of scale-up parameters for industrial manufacturing.

11. CONCLUSION

Murraya koenigii represents a scientifically compelling candidate as a natural pharmaceutical excipient for effervescent antacid tablet formulations. The leaf-derived mucilage demonstrates multifunctional excipient properties — binding, disintegrant, and mucoadhesive functionalities — that are physically and mechanistically complementary to the requirements of effervescent tablet technology. Crucially, the intrinsic pharmacological activity of *M. koenigii* phytoconstituents, encompassing anti-ulcer, anti-secretory, carminative, and anti-*H. pylori* effects mediated through multiple molecular targets, offers the prospect of formulation-pharmacology synergy that cannot be achieved with conventional synthetic excipients. The physicochemical characterization data reviewed — acceptable Carr's index, swelling index, viscosity, and thermal stability — confirm basic excipient suitability. The *in vitro* formulation performance data, including disintegration times of 55–90 seconds, acid-neutralizing capacity of 18–22 mEq/tablet, and pH elevation to 6.2–6.8 from a simulated fasting gastric pH of 1.2, indicate a clinically meaningful antacid response meeting compendial specifications. The favorable safety profile ($LD_{50} > 5000$ mg/kg, no genotoxicity) and long history of food and medicinal use further support the safety basis for human application. The primary challenges — batch variability, hygroscopicity management, lack of compendial monograph, and insufficient clinical evidence — are recognized but addressable through targeted research, investment in cultivation and extraction

standardization, and engagement with regulatory agencies via novel excipient pathways. Given the global resurgence of interest in plant-based medicines, natural excipients, and sustainable pharmaceutical manufacturing, *M. koenigii* holds significant promise as a next-generation natural excipient aligned with the green pharmacy paradigm. A coordinated research effort encompassing phytochemistry, pharmaceutical technology, clinical pharmacology, and regulatory science is warranted to fully realize this potential.

Declarations

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