Study Of the Synergistic Anti-Inflammatory Activity of Leaves of Abelmoschus Esculentus and Momordica Dioica

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***Abstract*—This study intends to present the biological and chemical range of A. esculentus. This plant contains many vitamins, minerals, proteins, and carbohydrates in addition to flavonoids, terpenes, phenolic compounds, and sterols. Momordica dioica is a tuberous-rooted perennial dioecious climber that grows throughout India and the Indian subcontinent. It belongs to the Cucurbitaceae family. Alkaloids, steroids, triterpenoids, flavonoids, glycosides, saponins, and other bioactive substances have been identified through phytochemical investigation of M. dioica fruits. The fruit is rich in nutrients, containing high levels of carbohydrates, protein, lipids, fiber, minerals (calcium, iron, potassium, zinc, and sodium), and vitamins (carotene, thiamin, riboflavin, and niacin). Further research is needed to elucidate the specific mechanisms by which M. dioica exerts its anti-inflammatory and anti-diabetic effects and to explore its potential as a natural therapeutic agent for diabetes and other oxidative stress-related disorders. His combined use of leaves from these two plants presents a promising phytotherapeutic strategy for managing inflammation, warranting further preclinical and clinical investigation into fixed-dose combination formulations. The synergistic anti-inflammatory potential, combined with their safety profiles and nutritional value, makes these plants strong candidates for future anti-inflammatory drug development.**

***Index Terms*—Momordica dioica, Phytochemicals, Anti-inflammatory, Medicinal properties, Abelmoschus esculentus**

I. INTRODUCTION

Inflammation is a complex and highly regulated biological defense mechanism triggered by tissue injury, infection, or exposure to noxious stimuli. Mediated by a cascade of signaling molecules including prostaglandins, leukotrienes, interleukins, and tumor necrosis factor-alpha (TNF-α) inflammation serves as a critical component of the immune response. However, chronic or uncontrolled inflammation is recognized as a central pathological driver in a wide spectrum of diseases, including rheumatoid arthritis, inflammatory bowel disease, atherosclerosis, type 2 diabetes, neurodegenerative disorders, and various cancers (Kumar et al., 2010).

The global prevalence of inflammatory diseases is rising alarmingly. According to the World Health Organization (WHO), non-communicable diseases many of which have an inflammatory etiology account for approximately 71% of all deaths globally. Conventional pharmacological management of inflammation primarily relies on non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. While effective, these agents are associated with significant adverse effects, including gastrointestinal ulceration, renal toxicity, hepatotoxicity, cardiovascular risks, and immunosuppression, especially with long-term use (Vane and Botting, 1998). This pharmacovigilance burden has created an urgent need for safer, efficacious, and cost-effective alternatives.

Traditional and complementary medicine systems including Ayurveda, Unani, and traditional Chinese medicine have long employed medicinal plants to manage inflammatory conditions. The pharmacological basis for many of these traditional practices has now been substantiated by modern scientific investigations. Plants offer a rich,

structurally diverse reservoir of bioactive compounds with multi-target mechanisms of anti-inflammatory action, often with fewer side effects than synthetic drugs (Williamson, 2001).

The concept of synergism wherein the combined effect of two or more agents exceeds the sum of their individual effects is particularly relevant in plant-based medicine. Polyherbal formulations exploiting synergistic phytochemical interactions have demonstrated superior therapeutic outcomes in preclinical models. The rational selection of plant combinations based on complementary phytochemical profiles and non-overlapping mechanisms of action represents an emerging and scientifically sound approach to anti-inflammatory drug development (Wagner and Ulrich-Merzenich, 2009).

In this context, Abelmoschus esculentus (L.) Moench commonly known as okra or lady's finger and Momordica dioica Roxb. ex Willd.commonly known as spine gourd or teasel gourd are two botanically distinct but pharmacologically complementary medicinal plants. Both are widely consumed as vegetables across South and Southeast Asia and have deep roots in traditional medicine systems. Their leaves, in particular, are used locally for managing pain and inflammatory conditions. However, no systematic review has yet evaluated the synergistic anti-inflammatory potential of combining leaf extracts from both plants. The present review addresses this gap by consolidating the existing evidence base across phytochemistry, pharmacology, and ethnomedicine.

II. BOTANICAL AND TAXONOMIC DESCRIPTION

Abelmoschus esculentus (L.) Moench Okra

Abelmoschus esculentus, commonly known as okra, lady's finger, or bhindi, is an annual herbaceous plant belonging to the family Malvaceae. It is believed to have originated in the Ethiopian Highlands of Northeastern Africa, from where it spread to the Mediterranean region, the Middle East, and South Asia. Today, it is one of the most widely cultivated vegetables in tropical, subtropical, and warm temperate regions worldwide, with major production in India, Nigeria, Sudan, Pakistan, Ghana, and Egypt (Benchasri, 2012).

Figure 1: Abelmoschus esculentus (L.) Moench

The plant grows to 1–2 meters in height with broad, palmate, and somewhat hairy leaves that are deeply lobed. The flowers are large, yellow with a dark purple center, typical of the Malvaceae family. The fruit is an elongated, green, mucilaginous pod harvested before maturity. The leaves, though less studied than the fruit, are nutrient-dense and contain significant quantities of bioactive phytochemicals, making them pharmacologically relevant (Jain et al., 2012).

Taxonomic Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Class	Magnoliopsida
Order	Malvales
Family	Malvaceae
Genus	Abelmoschus Medik.
Species	A. esculentus (L.) Moench
Common Names	Okra, Lady's Finger, Bhindi, Vendakkai, Bamia

Table 1: Taxonomic Classification of Abelmoschus esculentus

Momordica dioica Roxb. Ex-Will d. Spine Gourd

Momordica dioica Roxb. Ex Willd. Is a perennial, dioecious, climbing herbaceous plant belonging to the family Cucurbitaceae. It is commonly known as spine gourd, teasel gourd, Karol, or Kantola. Native to the Indo-Malayan region, it is widely distributed across India, Bangladesh, Sri Lanka, Myanmar, China, Japan, Southeast Asia, Polynesia, Tropical Africa, and parts of South America. In India, it is cultivated in states such as Assam, West Bengal, Odisha, Jharkhand, Chhattisgarh, and Maharashtra, typically at altitudes up to 1500 meters (Talukdar et al., 2014).

Figure 2: Momordica dioica Roxb. Ex Willd. Spine Gourd

The plant is a slender climber reaching 5–7 meters in length, propagated by underground tubers. It is dioecious individual plants bear either male or female flowers. The leaves are small, cordate, and deeply lobed with a rough texture. The fruits are small, round or ovoid, dark green, and spiny when immature, turning yellow-orange upon ripening. As a traditional medicinal plant, all parts, including leaves, fruit, root, and tubers, have been used across multiple indigenous healthcare systems (Frontiers in Pharmacology, 2026).

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Cucurbitales
Family	Cucurbitaceae
Genus	Momordica L.
Species	M. dioica Roxb. ex Willd.
Common Names	Spine Gourd, Teasel Gourd, Kantola, Kakrol, Kankro, Kartoli

Table 2: Taxonomic Classification of Momordica dioica

III. MEDICINAL USES

Traditional Uses of Abelmoschus esculentus Leaves

In Ayurvedic and folk medicine, the leaves of A. esculentus have been employed for various medicinal purposes. Leaf poultices have traditionally been applied topically to reduce inflammation and as emollients for soothing skin conditions. Decoctions of dried leaves have been used in treating inflammatory bowel conditions and gastric ulcers. In West African traditional medicine, okra leaves are cooked and consumed regularly as a dietary measure against diabetes and chronic inflammatory conditions. In Turkey, the plant is used in traditional treatment of ulcers and gastritis, and its gastroprotective effects have now been validated in experimental models (Auctores, 2024).

Parameter	A. esculentus (Leaves)	M. dioica (Leaves)
System	Ayurveda, African TM, Turkish TM	Ayurveda, Folk medicine (India, BD)
Inflammation	Topical poultice; bowel inflammation	Joint pain, skin inflammation, lizard-sting
Pain	Arthritis decoction (with pepper)	Headache ointment, analgesic
Fever	Antipyretic in some regions	Antipyretic, antiasthmatic
Wound Healing	Wound poultice (Africa)	Topical inflammation
GI Disorders	Gastroprotective, antispasmodic	Antihemorroidal, laxative
Respiratory	Limited traditional use	Antibronchitic, antiasthmatic

Table 3: Comparative medicinal Uses of Both Plant Leaves

In India, especially in rural communities, fresh okra leaves are used as a demulcent, laxative, and antispasmodic. In Egypt and Sudan, okra leaves are applied as wound-healing agents and anti-inflammatory poultices. The mucilaginous nature of the leaves is attributed to their polysaccharide content, which forms a protective coating over inflamed tissues. In South India, okra leaves boiled with black pepper are consumed as a traditional remedy for joint pain and arthritis (Jain et al., 2012).

Traditional Uses of Momordica dioica Leaves

According to Ayurveda, M. dioica leaves possess anthelminthic, aphrodisiac, antitheoretical, hepatoprotective, antibronchitic, antipyretic, antiasthmatic, and analgesic properties. In traditional practice, leaf juice is mixed with coconut oil, pepper, and red sandalwood to prepare an ointment applied to the head to relieve pain. The leaves are also used to treat inflammatory skin conditions and headaches (Talukdar et al., 2014).

Tribal communities across Jharkhand, Chhattisgarh, and Odisha in India use fresh leaf juice of M. dioica to

relieve inflammation caused by contact with lizard excretions. The leaves are also used as antipyretics in febrile states and as analgesics in musculoskeletal pain. In Bangladesh, fresh leaf extracts are used by traditional healers to manage respiratory inflammation and bronchitis (PMC, 2014).

IV. PHYTOCHEMICAL PROFILE

Phytochemistry of Abelmoschus esculentus Leaves

The leaves of A. esculentus are phytochemically diverse, containing a broad spectrum of bioactive compounds. Flavonoids constitute a major class of anti-inflammatory phytochemicals present in okra leaves, with quercetin, rutin, isoquercitrin (quercetin-3-glucoside), and hyperoside being among the most well-characterized. Quercetin, in particular, is a potent inhibitor of NF-κB activation, COX-2 expression, and pro-inflammatory cytokine release (TNF-α, IL-1β, and IL-6), contributing substantially to the anti-inflammatory activity observed in okra leaf extracts (PMC, 2023).

Polysaccharides and pectin isolated from okra leaves and pods have demonstrated anti-inflammatory activity by reducing pro-inflammatory cytokine levels and modulating the gut immune environment. Okra pectin has been shown to reduce IL-8 and reactive oxygen species (ROS) in experimental ulcerative colitis models. The polyphenolic content of leaves includes caffeic acid, ferulic acid, gallic acid, and chlorogenic acid, which collectively suppress lipid peroxidation and modulate oxidative-inflammatory coupling. Catechins, another class of phenolics present, contribute to anti-arthritic effects through inhibition of matrix metalloproteinases (MMPs) (Xiong et al., 2021; MDPI, 2025).

The presence of β-sitosterol, a phytosterol known to inhibit prostaglandin synthesis and reduce vascular permeability, further reinforces the anti-inflammatory portfolio of okra leaves. Alkaloids, tannins, and terpenoids detected in phytochemical screening also contribute to anti-inflammatory and analgesic activities. Vitamins C and E serve as antioxidant cofactors that quench free radicals generated during inflammatory cascades, indirectly dampening the inflammatory response (RSC, 2023).

Phytochemical	Class	Mechanism of Action
Quercetin	Flavonoid	Inhibits NF-κB, COX-2; reduces TNF-α, IL-6
Rutin	Flavonoid glycoside	Antioxidant; inhibits lipoxygenase; reduces vascular permeability
Isoquercitrin	Flavonoid glycoside	COX inhibition; cytokine suppression
Caffeic Acid	Hydroxycinnamic acid	NF-κB inhibition; anti-oxidative
Okra Pectin	Polysaccharide	Reduces IL-8, ROS; gut mucosal protection
β-Sitosterol	Phytosterol	Inhibits prostaglandin synthesis
Catechins	Flavan-3-ol	MMP inhibition; anti-arthritic
Chlorogenic Acid	Phenolic acid	COX inhibition; antioxidant
Tannins	Polyphenol	Wound healing; anti-inflammatory
Vitamin C, E	Vitamins	Radical scavenging; indirect anti-inflammatory

Table 4: Major Phytochemicals in Abelmoschus esculentus Leaves and Their Anti-Inflammatory Relevance

Phytochemistry of Momordica dioica Leaves

The leaves of M. dioica contain a distinct and pharmacologically potent set of phytochemicals. Cucurbitacins particularly cucurbitacin B and related triterpenoids are among the most prominent anti-inflammatory constituents. Cucurbitacin B suppresses the NF-κB signaling pathway, reduces COX-2 expression, and inhibits STAT3 phosphorylation, all of which are key mediators of chronic inflammation. These mechanisms are distinct from, and therefore complementary to, those of flavonoids in A. esculentus leaves (Ask-Ayurveda, 2025).

Mordaciids I and II steroidal glycosides unique to Momordica species have been shown to modulate insulin receptor sensitivity and reduce inflammatory signaling in metabolic inflammation. Flavonoids quercetin and kaempferol are present in the leaves and provide antioxidant protection while inhibiting 5-lipoxygenase (5-LOX), an enzyme responsible for leukotriene synthesis. Oleanolic acid and ursolic acid, pentacyclic triterpenoids found in leaf extracts, are

well-established inhibitors of NF-κB and AP-1 transcription factors (Talukdar et al., 2014; ResearchGate, 2024).

Saponins, alkaloids (momordicin), and α-spinasterol in the leaves contribute additional anti-inflammatory, analgesic, and antipyretic properties. The ethanolic and aqueous leaf extracts of M. dioica have demonstrated hepatoprotective activity through reduction of oxidative stress markers (MDA, GSH), which is indirectly relevant to inflammatory liver conditions. Hederagenin, a triterpene saponin, has been identified in leaf fractions and is known to inhibit arachidonic acid metabolism (PMC, 2014).

Phytochemical	Class	Mechanism of Action
Cucurbitacin B	Triterpenoid	NF-κB inhibition; COX-2 suppression; STAT3 inhibition
Momordicoside I & II	Steroidal glycoside	Modulates insulin receptor; anti-metabolic inflammation
Quercetin	Flavonoid	5-LOX inhibition; NF-κB; anti-cytokine
Kaempferol	Flavonoid	Anti-inflammatory; antioxidant; 5-LOX inhibitor
Oleanolic Acid	Pentacyclic triterpene	NF-κB inhibition; AP-1 suppression
Ursolic Acid	Pentacyclic triterpene	COX/LOX inhibition; cytokine suppression
α-Spinasterol	Phytosterol	Antiproliferative; anti-inflammatory
Hederagenin	Triterpene saponin	Arachidonic acid metabolism inhibition
Momordicin	Alkaloid	Analgesic; anti-inflammatory
Saponins	Glycoside	Antipyretic; anti-inflammatory

Table 5: Major Phytochemicals in Momordica dioica Leaves and Their Anti-Inflammatory Relevance

V. ANTI-INFLAMMATORY PHARMACOLOGICAL ACTIVITY

In Vitro Anti-Inflammatory Studies A. esculentus Leaves

Multiple in vitro studies have established the anti-inflammatory potential of A. esculentus leaf extracts. Ethanolic and methanolic extracts have demonstrated significant inhibition of protein denaturation a hallmark of anti-inflammatory activity in a concentration-dependent manner in albumin denaturation assays. The inhibition of heat-induced protein denaturation at concentrations of 100–500 µg/mL has been reported to exceed 60–70%, comparable to standard NSAIDs such as diclofenac sodium (PMC, 2023).

Quercetin and rutin isolated from okra leaves have demonstrated potent inhibition of COX-1 and COX-2 enzymes in cell-free assays. Quercetin exhibits IC50 values in the range of 1–10 µM for COX-2 inhibition, with notable selectivity for COX-2 over COX-1, suggesting an aspirin-like profile with potentially lower gastric side effects. Additionally, aqueous leaf extracts have shown significant inhibition of nitric oxide (NO) production in LPS-stimulated RAW 264.7 macrophages, with reductions in inducible nitric oxide synthase (iNOS) expression at concentrations of 200–400 µg/mL (MDPI, 2025).

Okra pectin, isolated from leaves and pods, has demonstrated inhibition of pro-inflammatory cytokines IL-8 and TNF-α in intestinal cell lines, establishing a mechanistic basis for the traditional use of okra in inflammatory bowel conditions. Free radical scavenging activity by DPPH assay showed IC50 values of 42–86 µg/mL for methanolic leaf extracts, with antioxidant activity positively correlated with anti-inflammatory outcomes (RSC, 2023).

In Vivo Anti-Inflammatory Studies A. esculentus Leaves

Carrageenan-induced paw edema in Wistar rats the gold standard model for acute inflammation has been extensively used to evaluate A. esculentus leaf extract activity. Methanolic leaf extract at oral doses of 200 and 400 mg/kg body weight produced significant ($p < 0.01$) reduction in paw volume by 44.3% and 57.8%, respectively, at the 3-hour mark, compared to 63.2% inhibition with indomethacin (10 mg/kg). The ethanolic extract also demonstrated significant anti-inflammatory activity in the cotton pellet granuloma model (chronic inflammation), suggesting efficacy against both acute and chronic inflammatory phases (Wiley, 2018).

Acetic acid-induced writhing tests (a model of visceral pain-inflammation) in mice showed significant ($p<0.05$) reduction in writhing responses at doses of 100 and 200 mg/kg of both methanolic fruit and seed

extracts, which is extrapolable to leaf fractions with similar phytochemical composition. Histological analysis of inflamed tissue treated with okra leaf extracts revealed reduced inflammatory cell infiltration, decreased edema, and preserved epithelial architecture compared to untreated controls (Auctores, 2024).

In Vitro Anti-Inflammatory Studies M. dioica Leaves
Leaf extracts of M. dioica have shown robust in vitro anti-inflammatory activity across multiple assay systems. In a comparative study involving three Momordica species, leaf extract of M. dioica demonstrated the highest anti-inflammatory activity, positively correlated with its total phenolic content (TPC) and total flavonoid content (TFC) (ScienceDirect, 2014).
Cucurbitacin B from M. dioica leaves has been shown to inhibit NF-κB translocation to the nucleus in TNF-α-stimulated cells, effectively suppressing downstream transcription of inflammatory genes, including COX-2, iNOS, and pro-inflammatory cytokines (IL-1β, IL-6, IL-8). Kaempferol and quercetin isolated from leaves exhibit 5-LOX inhibitory activity (IC50 ~ 4.2 μM for kaempferol), reducing leukotriene B4 (LTB4) synthesis, a potent chemotactic mediator of neutrophil recruitment in inflammation (Ask-Ayurveda, 2025).

In Vivo Anti-Inflammatory Studies M. dioica Leaves
Significant in vivo anti-inflammatory evidence exists for M. dioica leaf extracts. Leaf extract at 200 mg/kg body weight produced significant inhibition of carrageenan-induced paw edema in Wistar rats, with anti-inflammatory activity comparable to indomethacin at 10 mg/kg, the reference standard. Percentage edema inhibition of approximately 55–60% was reported at 3 hours post-carrageenan injection, with the methanol extract demonstrating superior activity over aqueous or hexane fractions (ScienceDirect, 2014).
In formaldehyde-induced arthritis models—relevant to chronic inflammatory joint disease M. dioica leaf extract at 300–400 mg/kg significantly reduced paw volume, improved joint mobility markers, and reduced serum inflammatory markers (CRP and ESR) compared to arthritic control animals. Analgesic activity assessed by hot plate and tail flick tests further confirmed the anti-nociceptive component of the anti-inflammatory profile (Ilango et al., 2003).

Plant	Extract	Model	Dose / Activity
A. esculentus	MeOH leaf	Carrageenan paw edema	200–400 mg/kg; 44–58% inhibition
A. esculentus	Aqueous	LPS macrophage (in vitro)	200–400 μg/mL; ↓ NO, iNOS, TNF-α
A. esculentus	Pectin	Ulcerative colitis (in vivo)	400–800 mg/kg; ↓ IL-8, ROS, MDA
A. esculentus	EtOH / MeOH	Protein denaturation (in vitro)	60–70% inhibition @ 500 μg/mL
M. dioica	MeOH leaf	Carrageenan paw edema	200 mg/kg; ~55–60% inhibition
M. dioica	Leaf (multi-fraction)	Comparative Momordica species study	Highest TPC, TFC; highest anti-inflammatory
M. dioica	MeOH leaf	Formaldehyde arthritis	300–400 mg/kg; ↓ CRP, ESR, joint volume
M. dioica	Leaf (cucurbitacin B)	NF-κB pathway (in vitro)	↓ COX-2, iNOS, IL-1β, IL-6, IL-8

Table 6: Summary of Anti-Inflammatory Studies A. esculentus and M. dioica Leaves

VI. SYNERGISTIC ANTI-INFLAMMATORY POTENTIAL

Scientific Rationale for Combining Both Leaves
Synergism in pharmacology is defined as the interaction between two or more agents producing a combined effect greater than the sum of their individual effects. In herbal medicine, synergism can arise through complementary mechanisms (multi-target action), pharmacokinetic interactions (enhanced bioavailability), or additive phytochemical content of shared active compounds.
The combination of A. esculentus and M. dioica leaves presents a scientifically compelling synergistic profile based on the following rationale:

1. Complementary Mechanisms: A. esculentus predominantly targets COX-2 and NF-κB through flavonoid mechanisms, while M. dioica adds 5-LOX inhibition (kaempferol), STAT3 suppression (cucurbitacin B), and arachidonic acid pathway modulation (hederagenin, ursolic

acid). Together they achieve broader pathway coverage.

2. Shared Quercetin Content: Both plants independently contribute quercetin, resulting in additive NF-κB and COX-2 inhibition at the combination level, with the potential for sub-therapeutic individual doses achieving a therapeutic combined effect.
3. Dual COX-LOX Blockade: The combination avoids compensatory LOX upregulation seen with selective COX-2 inhibition alone.
4. Antioxidant Synergism: The combined pool of antioxidants (polyphenols, vitamins, cucurbitacins) provides superior ROS quenching compared to either plant alone, amplifying the anti-inflammatory effect.
5. Gut Mucosal Protection: A. esculentus pectin provides mucosal protection in the GI tract, potentially improving absorption and reducing gastric irritation from any active compounds, enhancing the overall tolerability of the combination.

VII. RESEARCH GAPS AND FUTURE DIRECTIONS

Despite the promising anti-inflammatory evidence reviewed above, several critical research gaps remain:

1 Direct Synergy Studies: No published preclinical study has directly evaluated the combined anti-inflammatory effect of A. esculentus and M. dioica leaf extracts using combination index (CI) or isobolographic analysis. Such studies are urgently needed to quantify synergistic interactions.

2 Bioavailability and Pharmacokinetics: ADME (Absorption, Distribution, Metabolism, and Excretion) profiles for key active compounds (cucurbitacin B and okra quercetin glycosides) have not been systematically characterized for leaf extracts.

3 Standardized Extracts: Development of quality-controlled, standardized leaf extract preparations with defined phytochemical markers is essential before clinical evaluation.

4 Clinical Trials: Human clinical trial data for the anti-inflammatory efficacy of both plant leaf extracts is virtually absent. Phase I/II trials assessing safety and efficacy in inflammatory conditions such as osteoarthritis, IBD, or metabolic inflammation are warranted.

5 Molecular Docking / In Silico Analysis: Computational studies evaluating binding affinities of key phytochemicals (cucurbitacin B, quercetin, kaempferol, and rutin) to inflammatory targets (COX-2, NF-κB, and 5-LOX) could provide valuable mechanistic insights and guide formulation development.

6 Optimal Ratio Studies: Identification of the optimal ratio of A. esculentus to M. dioica leaf extract in a combination formulation, balancing efficacy and safety, requires systematic dose-optimization studies.

7 Formulation Development: Development of standardized polyherbal formulations (tablets, capsules, topical gels) incorporating both leaf extracts, with appropriate excipients to enhance bioavailability and stability.

VIII. CONCLUSION

This comprehensive review has systematically evaluated the phytochemistry, ethnomedicinal history, pharmacological anti-inflammatory activity, and synergistic potential of leaves of Abelmoschus esculentus (L.) Moench and Momordica dioica Roxb. ex Willd. The evidence strongly supports that both plants possess well-characterized, multi-mechanistic anti-inflammatory activity through complementary molecular pathways.

A. esculentus leaves offer a rich portfolio of flavonoids (quercetin, rutin, and isoquercitrin), polyphenols, mucilaginous polysaccharides, and pectin, demonstrating significant NF-κB inhibition, COX-2 suppression, and cytokine reduction, particularly in models of gut inflammation. M. dioica leaves contribute cucurbitacin's (especially cucurbitacin B), mordaciids, ursolic acid, oleanolic acid, kaempferol, and saponins targeting STAT3, AP-1, 5-LOX, and COX/LOX pathways with potent edema and joint inflammation suppression.

The synergistic anti-inflammatory rationale for combining both plant leaves rests on complementary pathway targeting, additive quercetin content, dual COX-LOX blockade, and superior combined antioxidant capacity. Collectively, this combination may offer anti-inflammatory efficacy superior to either plant alone, potentially at lower doses, thereby

improving the therapeutic index over conventional NSAIDs.

Both plants carry favorable safety profiles based on long dietary use histories and available toxicological data. The principal knowledge gaps absence of direct synergy studies, lack of human clinical data, and limited pharmacokinetic characterization represent tractable and high-priority research objectives.

In conclusion, the combined leaf formulation of A. esculentus and M. dioica emerges as a scientifically promising, culturally validated, and practically accessible candidate for the development of a safe, effective, and affordable herbal anti-inflammatory therapeutic. Future well-designed preclinical synergy studies and clinical trials are strongly recommended to translate this promising phytotherapeutic concept into evidence-based medicine.

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