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Pharmacological horizons of *Alhagi maurorum*: A narrative exploration of its anti-oxidant, anti-inflammatory, anti-apoptotic, anticancer, and immunomodulatory dimensions

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ABSTRACT

Alhagi maurorum Medik. (*A. maurorum*), belonging to the Fabaceae family, a desert-adapted botanical with deep ethnomedicinal roots, has recently garnered attention for its multifaceted pharmacologic potential. This narrative review explores the anti-oxidant, anti-inflammatory, anti-apoptotic, anticancer, and immunomodulatory properties of *A. maurorum*, emphasizing its mechanistic depth and translational relevance across preclinical contexts. A systematic literature search was conducted until June 2026 using multiple scientific databases, including Google Scholar, PubMed, and Scopus. *In vitro* and *in vivo* studies investigating the pharmacological effects and mechanistic pathways of *A. maurorum* were searched. The evidence demonstrates that *A. maurorum* exerts anti-oxidant activity via ROS scavenging and Nrf2/HO-1 mediated up-regulation of endogenous defenses. Its anti-inflammatory effects stem from NF-κB and COX-2, coupled with enhanced expression of IL-4 and IL-10. Immunomodulation is achieved through mucosal immune engagement, IgA transport, dendritic cell maturation, and T-helper cell modulation. Anti-apoptotic effects are driven by caspase suppression, Bax down-regulation, and Bcl-2 up-regulation, while anticancer properties include selective cytotoxicity, anti-metastatic signaling inhibition, and nanoparticle biosynthesis for targeted delivery. By integrating traditional botanical knowledge with molecular pharmacology, *A. maurorum* emerges as a transdisciplinary candidate for future biotherapeutic development. Its systemic efficacy, mechanistic versatility, and ecological adaptability collectively position it as a promising agent in the advancement of evidence-based integrative medicine. However, future research must address pharmacokinetics, dose optimization, and safety profiling. Well-designed clinical trials are urgently needed to validate efficacy, assess long-term tolerability, and guide standardized formulation development.

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Introduction

Human chronic pathologies rarely stem from a singular molecular disturbance; rather, they emerge from a complex network of interdependent biochemical dysregulations (1). At the forefront of these perturbations lies oxidative stress, a condition arising when reactive oxygen and nitrogen species (ROS/RNS) are generated in quantities that surpass the neutralizing capacity of intrinsic anti-oxidant defenses (2). The resultant redox imbalance precipitates a cascade of cellular injuries, including lipid membrane disruption, nucleic acid fragmentation, and protein misfolding, collectively undermining cellular architecture and physiological performance (3). Far from functioning in isolation, oxidative stress is tightly interwoven with inflammatory signaling pathways (4, 5). ROS, through their modulatory effects, enhance the activation of redox-sensitive transcription factors such as nuclear factor kappa B (NF-κB) and activator protein 1 (AP-1) (6, 7). This leads to the transcriptional amplification of inflammatory mediators including tumor necrosis factor-alpha (TNF-α), interleukins (IL)-6, IL-1β, chemokines, and adhesion molecules, all of which act synergistically to intensify and spatially anchor the inflammatory response (8, 9).

As inflammatory processes persist, they begin to disrupt the finely tuned balance of apoptotic regulation and immune system functionality (10). Aberrant activation of caspases,

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along with altered mitochondrial membrane permeability, promotes premature apoptosis in immune cells, a disruption that compromises tissue repair and destabilizes cellular homeostasis (11). In parallel, this apoptotic dysregulation facilitates the survival of genetically abnormal cells that evade immunological detection, a vulnerability further aggravated by systemic immune dysfunction (12). The immunological dysfunction is reflected in an imbalanced distribution of T cell subsets, impaired surveillance by dendritic cells, and increased expression of immune-inhibitory checkpoints that facilitate tumor growth (13). As a result, the immune system may become either ineffective or, paradoxically, contribute to cancer development (14).

Cancer involves a complex interplay of oxidative stress, persistent inflammation, disrupted apoptosis, and immune evasion. Within the tumor microenvironment, these processes converge: oxidative deoxyribonucleic acid (DNA) damage drives genomic instability, inflammation promotes progression, apoptotic failure ensures cell survival, and compromised immunosurveillance allows for tumor escape (15, 16). Importantly, this mechanistic interplay extends beyond oncology. Similar molecular disruptions underpin the pathogenesis of metabolic syndromes including diabetes (17), neurodegenerative diseases (18), cardiovascular pathologies (19), autoimmune disorders (20-22), and malignancies (23). Unraveling and therapeutically modulating this interconnected network of biological dysfunctions is essential for advancing precision medicine and designing innovative therapies with relevance across multiple disease states.

Considering the complexity of disease mechanisms, conventional monotherapies targeting single pathways often show limited efficacy in multifactorial conditions. Issues such as drug resistance, adverse effects, and limited accessibility have increased interest in integrative, biocompatible, and mechanistically versatile therapies. Medicinal plants and their bioactive compounds have long contributed to the prevention and treatment of diverse diseases (24). Among these, *Alhagi maurorum* (*A. maurorum*), commonly known as camelthorn, is a perennial Fabaceae shrub characterized by thorny, highly branched stems and an extensive root system. Its roots may reach depths of up to 15 m, supporting vegetative spread and ecological establishment in arid environments. For centuries, its roots, aerial parts, and sugary exudate known as manna have been used in traditional medicine across the Middle East, North Africa, and Central Asia, particularly for hepatic, gastrointestinal, and urinary disorders (25). Across traditional medical systems in Pakistan, Saudi Arabia, and Uzbekistan, *A. maurorum* has been employed in the treatment of a diverse array of conditions, including chronic ulceration, hemorrhoid inflammation, respiratory ailments such as cough, musculoskeletal discomforts like rheumatic pain and angina, as well as dermatological issues and gastric inflammation (26). Notably, the plant's manna has been historically credited with purgative, cleansing, and fever-reducing effects, as well as managing hepatic bile imbalances and pulmonary disorders (26). In Iran, *A. maurorum*, commonly referred to as KharShotor, has long been recognized for its medicinal properties. Traditionally, it has been employed to alleviate constipation due to its laxative effects, to clear respiratory passages as an expectorant, and to treat ailments related to the urinary tract. Additionally, it has been used to help neutralize excess stomach acid (27). In traditional Persian medicine, *A. maurorum*, known as "Hāj" or "Khar Shotor," is described as having a hot and very dry temperament. It has been traditionally used to relieve internal obstructions, counteract poisons, and treat hemorrhoids through infusions, topical preparations, or vapor. Its juice was also applied for mild ocular opacity, while nasal administration of its extract followed by violet oil inhalation was recommended for chronic phlegm. In addition, oil prepared from fresh leaves was used for joint pain and cold-natured conditions, and the flowers were considered beneficial for hemorrhoids (28, 29).

A. maurorum is increasingly recognized for its multifaceted pharmacological activities, most notably its anti-oxidant (30, 31), anti-inflammatory (32), anticancer (33), and immunomodulatory (34) effects. These bio-functional properties have made it an attractive candidate in the search for therapeutic agents targeting oxidative stress, chronic inflammation, and immune system dysregulation.

A diverse array of bioactive compounds has been extracted from *A. maurorum*, including flavonoids and alkaloids such as naringenin 5-methyl ether 4-glucoside, quercetin, leucodelphinidin, gallocatechin, and epigallocatechin. Additional constituents like calsolidine, N-methylmescaline, hordenine, 3,4-dihydroxy-phenethyltrimethylammonium hydroxide, and N-methylphenethylamine have also been identified. Further phytochemical investigations revealed the presence of isorhamnetin, kaempferol variants, and chrysoeriol derivatives. Moreover, key phenolic compounds such as hydroxybenzoic acid, coumaric acid, cinnamic acid, and beta-sitosterol have been recognized as major constituents of this plant (27).

Preclinical evidence suggests that effective *in vivo* doses of *A. maurorum* commonly range from 100 to 500 mg/kg, depending on the extract, model, and administration route (35). In humans, limited clinical evidence has reported the use of 1 g/day hydroalcoholic aerial extract for 2 weeks without significant complications in patients with kidney and upper ureteral stones (36). However, current data remain insufficient to establish a standardized safe human dose range.

This review critically examines current scientific findings on the pharmacological effects of *A. maurorum*, with a focus on its anti-oxidant, anti-inflammatory, anti-apoptotic, anti-cancer, and immune-regulating properties. By outlining the molecular and cellular mechanisms behind these actions, it highlights the therapeutic potential of *A. maurorum* as a natural agent in modern biomedical and pharmacological contexts. A clearer understanding of these pathways may inform new strategies for preventing and managing disorders driven by oxidative stress, chronic inflammation, apoptosis, and immune imbalance.

Methods

A systematic literature search was conducted until June 2026 using multiple scientific databases, including Google Scholar, PubMed, and Scopus. The search strategy employed targeted keywords such as "camelthorn", "*Alhagi maurorum*", "Taranjabin", and mechanistic descriptors like "anti-inflammation", "inflammation", "anti-inflammatory", "inflammatory", "oxidative stress", "anti-oxidant", "oxidative damage", "oxidative injury", "anti-apoptotic", "apoptosis", "apoptotic", "immunomodulatory", "immunoregulatory", "immune system", "anti-tumor", "anti-cancer", "cancer", and "malignancy", specifically within article titles. Only English-language publications appearing in peer-reviewed journals were considered eligible for inclusion.

The selection criteria prioritized studies that: (1) investigated the anti-oxidant, anti-inflammatory, anti-

apoptotic, anti-cancer, or immunomodulatory properties of *A. maurorum* or its isolated constituents across *in vitro*, *in vivo*, or clinical models; (2) elucidated mechanistic pathways or molecular targets underlying these effects; and (3) utilized either purified *A. maurorum*-derived compounds or standardized extracts of *A. maurorum*. Studies were excluded if they: (1) focused on species other than *A. maurorum*; (2) combined *A. maurorum* with other pharmacological agents or botanical substances; or (3) comprised secondary literature such as reviews, meta-analyses, letters, editorials, or conference abstracts.

Results

Anti-oxidant effects

Metabolic pathways with both catabolic and anabolic roles, particularly the tricarboxylic acid cycle and the mitochondrial electron transport chain, are major sources of ROS, generating free radicals as byproducts of energy metabolism (37). Oxidative stress occurs when ROS production exceeds the body's anti-oxidant defense capacity, resulting in cellular dysfunction and tissue damage (38). As oxidative markers accumulate, they provoke the degradation of key biomolecules, namely nucleic acids, proteins, and lipids, thereby fueling the progression of disorders linked to oxidative imbalance (39). A growing body of evidence implicates oxidative stress as a pathogenic factor in a broad spectrum of diseases, including diabetes (40, 41), cardiovascular pathologies (42), neurodegenerative conditions (43), oncogenesis (23, 44), and the biological processes underlying aging (45).

In response to elevated ROS levels and oxidative damage, cells initiate adaptive defense mechanisms aimed at preserving homeostasis and preventing further injury. This involves a tightly regulated network of molecular sensors and transcriptional activators that modulate gene expression in favor of cytoprotection (46). Among these, redox-sensitive signaling pathways, most notably those involving nuclear factor erythroid 2-related factor 2 (Nrf2) and NF-κB, play central roles in orchestrating cellular resilience and survival under stress conditions. Nrf2 is a pivotal redox-sensitive transcription factor that regulates cellular defense by activating anti-oxidant genes via the anti-oxidant response element (ARE) enhancer, particularly under oxidative stress. Its activity is modulated through Kelch-like ECH-associated protein 1 (Keap1) interactions, epigenetic cues, and phosphoinositide 3-kinases (PI3K)/protein kinase B (Akt) signaling. Similarly, NF-κB coordinates inflammatory and stress responses, with canonical and noncanonical pathways directing gene transcription via dynamic dimerization and inhibitor of kappa B (IκB) regulation (47).

To counteract the detrimental effects of oxidative stress, cells are equipped with a sophisticated anti-oxidant network comprising both enzymatic and non-enzymatic systems. Key enzymatic anti-oxidants include superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), which operate in concert to detoxify ROS (46). SOD catalyzes the dismutation of superoxide anions into hydrogen peroxide, which is subsequently decomposed into water and oxygen by CAT (48). Simultaneously, GPx uses reduced glutathione (GSH) as a substrate to eliminate hydrogen peroxide and lipid peroxides, maintaining cellular redox homeostasis (49, 50). Non-enzymatic anti-oxidants, such as vitamins C and E, and polyphenols, also scavenge free radicals and modulate redox signaling (46).

Due to this complex involvement, bioactive compounds with anti-oxidant capabilities have emerged as promising therapeutic candidates for managing oxidative stress-associated conditions (51). Among natural sources, several herbal medicines have garnered attention for their potent anti-oxidant properties. The following section will explore current experimental and clinical findings on the anti-oxidant activities of *A. maurorum*, highlighting its therapeutic relevance in the context of oxidative stress-related pathologies.

In vitro

Platelets

In an *in vitro* study exploring the anti-oxidant potential of *A. maurorum*, the phenolic-rich root fraction was evaluated for its capacity to counteract oxidative damage in human plasma and platelets exposed to hydrogen peroxide (H_2O_2). Treatment with *A. maurorum* extract significantly attenuated protein oxidation-as indicated by preserved thiol group levels-and suppressed lipid peroxidation, evidenced by reduced thiobarbituric acid reactive substances (TBARS). Compared to commercial phenolic extracts (from resveratrol, *Yucca schidigera*, and *Aronia melanocarpa*), *A. maurorum* showed superior anti-oxidant properties, although differences were not statistically significant (52).

In vivo

Digestive system

In a rat model of aspirin-induced gastric injury, ethanolic extract of *A. maurorum* demonstrated protective effects comparable to ranitidine. The extract significantly attenuated gastric acid output and oxidative stress markers such as malondialdehyde (MDA), while restoring GSH levels. Both plant extract and ranitidine preserved liver enzyme profiles, improved lipid risk ratios, and reduced β-glucosidase, a tumor-associated glycosidase (53).

A. maurorum aqueous extract exerted a robust hepatoprotective effect against norfloxacin-mediated oxidative insult. Co-treatment led to significant reductions in serum alkaline phosphatase and transaminases (AST, ALT), indicative of attenuated hepatic damage. Enhanced anti-oxidant enzyme activities and reduced lipid peroxidation levels within hepatic tissue confirmed its oxidative stress-modulating capabilities. Histological evaluations corroborated these findings, showing near-normal liver histo-architecture and absence of necrotic or inflammatory changes in rats receiving both norfloxacin and the plant extract (54).

In a murine model of cyclophosphamide-induced toxicity, Alhagi honey-derived polysaccharides exhibited pronounced protective effects on both immune and intestinal systems. Alhagi honey-derived polysaccharides treatment counteracted cyclophosphamide-mediated immunosuppression by preserving spleen and thymus indices, maintaining body weight, and enhancing Peyer's patch counts. Cytokine analysis revealed elevated serum levels of IL-2, IL-6, and TNF-α, indicating an immunostimulatory response. On the intestinal front, Alhagi honey-derived polysaccharides significantly improved anti-oxidant status, as evidenced by increased SOD activity and β-defensin expression, alongside reductions in MDA and diamine oxidase levels, thereby mitigating oxidative and enzymatic damage. Furthermore, Alhagi honey-derived polysaccharides restored gut epithelial integrity, reversing CY-induced declines in villus architecture and immune cell populations, and normalizing the expression of tight junction and mucosal barrier proteins (zonula occludens-1 (ZO-1), mucin-2, E-cadherin, and occludin), as well as short-chain

fatty acid levels. Mechanistically, Alhagi honey-derived polysaccharides modulated mitogen-activated protein kinase (MAPK) signaling by enhancing phosphorylated extracellular signal-regulated kinase (p-ERK) expression while suppressing phosphorylated c-Jun N-terminal kinase (p-JNK) and p-p38 activation, suggesting a pathway-level attenuation of cyclophosphamide toxicity (55).

Administration of *A. maurorum* ethanolic extract significantly mitigated oxidative stress in mice subjected to concanavalin A-induced hepatitis. *A. maurorum* ethanolic extract treatment led to a marked reduction in hepatic levels of nitric oxide (NO), MDA, and NF-κB signaling, while effectively restoring GSH concentrations (56).

Dietary supplementation with *A. maurorum* powder at graded concentrations to rats with carbon tetrachloride (CCl_4)-induced hepatotoxicity resulted in dose-dependent hepatoprotective effects. Treated subgroups exhibited significant improvements in both body and liver weights, alongside notable reductions in serum markers of hepatic injury, including ALT, AST, alkaline phosphatase (ALP), and total bilirubin. At the oxidative level, *A. maurorum* supplementation markedly decreased hepatic MDA concentrations and enhanced GSH content (57).

A study on broiler chickens evaluated the effects of dietary supplementation with *A. maurorum* essential oil on intestinal morphology and anti-oxidant status. Supplementation with different levels of *A. maurorum* essential oil improved jejunal structure compared with the control diet, as reflected by increased villus height and a higher villus height-to-crypt depth ratio. These changes suggest enhanced intestinal absorptive surface area and potentially improved digestive efficiency. In addition, higher supplementation levels, particularly 0.75% and 1%, significantly increased CAT activity and total anti-oxidant capacity, indicating strengthened anti-oxidant defense mechanisms (58).

Endocrine system

Administration of aqueous and ethanolic extracts of *A. maurorum* to streptozotocin-induced diabetic rats significantly mitigated the metabolic and oxidative disturbances associated with diabetes mellitus. Both extracts attenuated hyperglycemia and dyslipidemia, MDA, and bilirubin, alongside decreased transaminase and glutathione reductase activities. Despite persistent insulin deficiency, the extracts restored anti-oxidant defenses by elevating SOD, GPx, glutathione S-transferase (GST) activities and GSH levels. Histopathological assessments also revealed diminished hepatic damage (59).

Nervous system

Aqueous extract of *A. maurorum* administered at graded doses exhibited notable analgesic and anti-oxidant effects. The extract significantly attenuated formalin-induced paw edema in a dose-dependent manner across both neurogenic and inflammatory phases, paralleling the efficacy of diclofenac sodium. Analgesic action was supported by reduced licking behavior during both early and late phases of formalin exposure. Anti-oxidant evaluation revealed a marked decline in MDA levels and enhanced total anti-oxidant capacity, comparable to acetylsalicylic acid (60).

In a study exploring the neuroprotective effects of *A. maurorum* ethanolic extract in lead-exposed rats, daily administration of the extract markedly mitigated lead-induced toxicity. Lead exposure triggered behavioral disturbances, including heightened locomotor activity and sensorimotor deficits, alongside reduced dopamine levels in the brain. Biochemically, it induced histopathological damage in brain tissue. These effects were accompanied by pronounced oxidative stress, evidenced by increased MDA and down-regulated anti-oxidant defenses, specifically reduced GSH, suppressed enzymatic activity, and lower messenger ribonucleic acid (mRNA) expression of anti-oxidant genes. Co-treatment with *A. maurorum* extract counteracted these disruptions, restoring anti-oxidant balance (61).

Ethanolic extract of *A. maurorum* showed substantial neuroprotective efficacy in a rat model investigating topiramate-induced neurotoxicity. Topiramate exposure led to elevated levels of oxidative stress markers neurospecific enolase, s100, serum phosphorylated neurofilament-H, and acetylcholinesterase, as well as diminished transcriptional expression of anti-oxidant genes in sciatic nerve tissue. Histopathological analysis revealed structural nerve damage, increased nitrotyrosine expression, and altered myelin integrity. Conversely, co-administration of *A. maurorum* extract restored anti-oxidant gene expression and normalized oxidative and neural biomarkers, with no signs of neurotoxicity (62).

Renal system

Assessing the protective effects of *A. maurorum* against cisplatin-induced nephrotoxicity, the extract demonstrated significant anti-oxidant effects in rats. Cisplatin administration led to elevated serum creatinine, urea-nitrogen, and imbalanced renal electrolyte handling, alongside oxidative stress evidenced by increased MDA and reduced ferric-reducing anti-oxidant power (FRAP). Oral supplementation with *A. maurorum* ameliorated these biochemical abnormalities, restoring renal function markers and anti-oxidant capacity. Histological evaluation confirmed reduced kidney tissue damage in treated groups (63).

Concurrent administration of *A. maurorum* aqueous extract significantly alleviated norfloxacin-induced nephrotoxicity. The treatment notably reduced serum markers of kidney dysfunction, including urea, creatinine, and uric acid, suggesting improved renal filtration and reduced tissue injury. Anti-oxidant restoration was evident in the kidney tissues, where the extract reversed norfloxacin-induced elevations in MDA and restored the activities of CAT, GPx, and SOD. Histopathological analysis further supported these biochemical improvements, demonstrating preserved renal architecture and reduced cellular degeneration in the co-treated group (54, 64).

In a murine model of acetaminophen-induced nephrotoxicity, pre-treatment with ethanol extract of *A. maurorum* roots demonstrated a dose-dependent renoprotective effect. It mitigated the rise in serum urea and creatinine, indicating preserved renal function. Furthermore, *A. maurorum* extract significantly improved anti-oxidant status, evidenced by elevated levels of CAT, SOD, and GSH, counteracting oxidative stress triggered by acetaminophen exposure. Histological examination corroborated these findings, revealing reduced renal structural damage in *A. maurorum*-treated groups (65).

Dietary supplementation with *A. maurorum* bread in a CCl_4-induced nephrotoxicity model in rats demonstrated dose-dependent renoprotective and anti-oxidant effects. Rats exposed to CCl_4 exhibited elevated serum urea, creatinine, lipid parameters, and MDA, alongside

significant reductions in GPx and TAC. However, the administration of *A. maurorum* bread attenuated these biochemical alterations, restoring kidney function markers and enhancing anti-oxidant defenses (66).

Administration of *A. maurorum* extract demonstrated marked anti-oxidant effects in lead-exposed rats. Specifically, co-treatment with the extract significantly reduced MDA accumulation in renal tissues. This anti-oxidant protection was further substantiated by the restoration of GSH levels and the enzymatic activities of CAT and SOD, both of which were depleted following lead intoxication. The extract's phenolic profile (quercetin, rutin, and orientin) likely contributed to its ability to scavenge ROS and preserve redox balance in the kidneys. At the molecular level, *A. maurorum* up-regulated Nrf2 and heme oxygenase-1 (HO-1) expression, indicating activation of the endogenous anti-oxidant response. In parallel, the extract suppressed NF-κB activity (67).

Reproductive system

Oral administration of hydro-ethanolic extract of *A. maurorum* to rats with testosterone-induced benign prostatic hyperplasia demonstrated significant protective effects. The extract notably reduced prostate weight and prostatic index, lowered both serum and tissue testosterone levels, and down-regulated the expression of 5-α-reductase and androgen receptor genes. Additionally, it enhanced TAC and diminished MDA levels in prostatic tissue (68).

Systemic oxidative stress

In growing Sindhi camels, dietary supplementation with *A. maurorum* enhanced systemic anti-oxidant defenses. Specifically, camels fed *A. maurorum*-containing diets showed reduced plasma MDA alongside elevated TAC. Moreover, GPx levels were significantly increased, with trends toward higher activities of SOD and CAT (69).

Assessing the dietary inclusion of *A. maurorum* in Japanese quail demonstrated its potential as a natural source of oxidative resilience. Birds receiving *A. maurorum* exhibited elevated serum anti-oxidant capacity, along with increased activities of key anti-oxidant enzymes, including GPx and SOD (70).

Supplementation with *A. maurorum*, particularly at 80% substitution for alfalfa, demonstrated a noticeable reduction in oxidative stress markers in growing ostriches. Chicks fed this level of Alhagi exhibited significantly lower plasma MDA concentrations, indicating reduced lipid peroxidation, and elevated plasma magnesium levels, a mineral known to support anti-oxidant enzyme activity (71).

In a study evaluating the physiological impacts of Alhagi honey-derived small-molecule sugars on Hu lambs, oral supplementation in the high-dose group yielded notable enhancements in redox regulation. Lambs receiving Alhagi honey–derived small molecule sugars at high dose exhibited significantly elevated serum levels of endogenous anti-oxidant enzymes, including TAC, GPx, and SOD, compared to controls (72).

Table 1. Summary of anti-oxidant activities of *Alhagi maurorum* in experimental model

Compound	Study design	Dose, duration	Results	Ref.
		In vitro		
Camelthorn phenolic fraction	Human platelets and plasma exposed to H_2O_2	0.5–50 µg/ml, 5 min	↓Protein oxidation, lipid peroxidation, TBARS	(52)
		In vivo		
CEE	Aspirin-induced gastric ulcers in rats	100 mg/kg, 10 days, PO	↑GSH ↓ gastric acid output, MDA	(53)
CAE	Norfloxacin-induced hepatotoxicity in rats	300 mg/kg, 14 days, PO	↑ antioxidant enzyme activities ↓ AST, ALT, lipid peroxidation in hepatic tissue	(54)
CEE	Concanavalin A-induced hepatitis in mice	300 mg/kg, 5 days, PO	↑ GSH ↓ hepatic NO, MDA, and NF-κB signaling	(56)
CP	CCL_4- induced hepatotoxicity in rats	2.5, 5, 10 % diet, 4 weeks, PO	↑ GSH ↓ ALT, AST, ALP, bilirubin, MDA	(57)
CAE and CEE	Streptozotocin-induced diabetes mellitus in rats	300 mg/kg, 4 weeks, PO	↑ SOD, GPx, GST activities, GSH ↓ hyperglycemia, dyslipidemia, MDA, bilirubin, TA and GR activities, hepatic damage	(59)
CAE	Formalin-induced paw edema in mice	125, 250, 500 µg/animal,	↑ analgesic, antioxidants, TAC ↓ paw edema, licking, MDA	(60)
CEE	Lead-induced neurotoxicity in rats	300 mg/kg, 3 months, gavage	↑ antioxidant genes, dopamine, GSH mRNA expression ↓ MDA, behavioral disturbances, histopathological damage	(61)
CEE	Topiramate-induced sciatic nerve injury in rats	300 mg/kg, 4 weeks, gavage	↑ Antioxidant gene expression	(62)
Camelthorn alcoholic Extract	Cisplatin-induced nephrotoxicity in rats	100 mg/kg, 10 days, PO	↑ FRAP ↓ serum creatinine, urea-nitrogen, MDA, tissue damage	(63)
CAE	Norfloxacin-induced nephrotoxicity in rats	300 mg/kg, 14 days, PO	↑ CAT, GPx, and SOD activities ↓ renal MDA, histopathological damages, urea, creatinine, uric acid	(54)

Continued Table 1.

CEE of roots	Acetaminophen-induced renal failure in mice	200, 400, 600 mg/kg, a week, PO	↑ CAT, SOD, GSH ↓ serum urea, creatinine	(65)
Camelthorn bread	CCl_4-induced nephrotoxicity	2.5, 5, 7.5, 10 %, 2 weeks, PO	↑ GPx, TAC ↓ serum urea, creatinine, MDA	(66)
Camelthorn hydro-ethanolic extract	Testosterone-induced benign prostatic hyperplasia in rats	200, 400 mg/kg, 28 days, gavage	↑ TAC ↓ 5-α reductase, ARGE, and MDA in prostatic tissue	(68)
CME	Lead-induced nephrotoxicity in rats	100, 200 mg/kg, 28 days, PO	↑ Renal GSH, CAT and SOD, Nrf2 and HO-1 expression ↓ renal MDA, NF-κB activity	(67)
Camelthorn	Addition of Camelthorn in growing camel diet	25 %, 50 % of diet, 150 days, PO	↑ TAC, SOD and CAT activity ↓ plasma MDA	(69)
CP of aerial parts	Addition of CP of aerial parts in Japanese quail chicks diet	1-4 % of diet, 21 days, PO	↑ serum anti[illegible]idant capacity, GPx and SOD [illegible]tivity	(70)
CP of aerial parts	Addition of CP of aerial parts in ostrich diet	20-100 % of diet, 6 weeks, PO	↑ [illegible]asma magnesium [illegible]ox[illegible]e stress markers, MDA, lipid peroxidation	(71)
CH	Administration of CH to Hu lambs	200- 800 mg/kg, 28 [illegible] PO	↑ redox regulation, serum TAC, GPx, SOD	(72)

ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TA: transa[illegible]inase; GA: glutathione reductase; CAE: camelthorn aqueous extract; CAT: catalase; CEE: Camelthorn ethanolic extract; CH: Camelthorn honey; CME: Camelth[illegible] methanolic [illegible]tract; CP: Camelthorn powder; FRAP: ferric reducing anti-oxidant power; GPx: glutathione peroxidase; GSH: glutathione; GST: glutathione S-transferase; HO-1: [illegible]me oxygenase-1; MDA: malondialdehyde; mRNA: messenger ribonucleic acid; NF-κB: nuclear factor kappa B; NO: nitric oxide; Nrf2: nuclear factor erythroid 2–related fac[illegible]or 2, [illegible].: per os (oral administration); Ref: reference; SOD: superoxide dismutase; TAC: total anti-oxidant capacity; TBARS: thiobarbituric acid reactive substances; ARGE: and[illegible]gen re[illegible]ptor genes expression

Table 1 presents a consolidated overview of the anti-oxidant effects of *A. maurorum*, highlighting its impact on oxidative stress biomarkers, enzymatic defenses, and tissue-level outcomes across various experimental models.

In general, the accumulated preclinical evidence positions *A. maurorum* as a versatile modulator of oxidative stress across a range of biological systems, with its efficacy anchored in a chemically rich profile of flavonoids, phenolics, and honey-derived oligosaccharides. Central to its protective capacity is its dual-action mechanism: direct scavenging of ROS and activation of endogenous anti-oxidant defenses through transcriptional regulation. Compounds such as quercetin, and orientin appear to operate synergistically, enhancing enzymatic anti-oxidants like SOD, CAT, and GPx, while restoring GSH levels and suppressing lipid peroxidation markers such as MDA. Regulatory engagement with redox-sensitive pathways, specifically up-regulation of Nrf2 and HO-1, and modulation of MAPK components including p-JNK and p-ERK, further suggests a capacity to influence cellular stress adaptation beyond ROS detoxification.

Importantly, *A. maurorum* exhibits system-wide adaptability, with demonstrated oxidative stress mitigation in hepatic, renal, neural, reproductive, intestinal, and hematologic contexts. This wide-ranging effect suggests that the different plant compounds may be working together in powerful ways, which deserves closer investigation using advanced methods like metabolomics and transcriptomics to understand how they influence biological processes. Nonetheless, methodological inconsistencies temper the interpretive strength of these findings. Variability in extract preparation (aqueous, ethanol, dietary, and honey-derived), lack of standardized dosing regimens, and limited use of comparator anti-oxidants confound cross-study validation. Few studies incorporate pharmacokinetic modeling or assess tissue distribution of bioactive compounds, leaving questions of bioavailability and clinical relevance unresolved. Moreover, while both aqueous and ethanol extracts show comparable efficacy in enzyme restoration, disparities in polyphenol yield highlight potential matrix effects and solubility-dependent bioactivity issues that demand standardization in future work.

From a translational perspective, the recurring success of *A. maurorum* interventions across rodent and livestock models is encouraging but incomplete. Moving forward, there is a critical need for dose-response exploration, time-course evaluations, and incorporation of human cell-based disease models. Clinical relevance will hinge on bridging bench-to-bedside gaps with rigorous trials assessing long-term safety, metabolic processing, and therapeutic outcomes. Particularly, the capacity of *A. maurorum* to suppress pro-oxidant signaling while up-regulating cytoprotective networks suggests promise in treating chronic, inflammation-linked conditions such as hepatic fibrosis, diabetic nephropathy, neurodegeneration, and mucosal damage. Its potential role in functional foods and integrative recovery protocols also warrants attention where anti-oxidant resilience could be supported via dietary enrichment rather than pharmacologic means alone.

Anti-inflammatory effects

Inflammation is a fundamental biological response triggered by cellular injury, toxic stimuli, or pathogenic invasion, with the intent to restore homeostasis (73). Inflammation, while a fundamental protective response, plays a pivotal role in the development of various diseases ranging from acute inflammatory reactions to chronic conditions-particularly when it becomes dysregulated or persists over time, leading to tissue damage in vital organs such as the lung (74), brain (75), liver (74), heart (76,

77), and kidneys (78). A central feature of this process is the activation of innate immune cells, which release pro-inflammatory mediators-including TNF-α and various interleukins (e.g., IL-1β, IL-6, IL-8)-that amplify the inflammatory cascade (79-81). These cytokines operate in concert with intracellular signaling pathways like MAPK and Janus kinase/signal transducer and activator of transcription (JAK/STAT), modulating gene expression and sustaining inflammatory responses (73, 82).

Pharmacological and botanical anti-inflammatory agents target this network to mitigate pathologic inflammation. *A. maurorum*, in particular, has gained attention for its ability to modulate these inflammatory drivers, offering promising results in experimental models. The next section will explore the anti-inflammatory potential of Alhagi extracts, highlighting both mechanistic insights and therapeutic relevance.

In vivo

Digestive system

In a comprehensive pharmacological investigation, the aerial parts of *A. maurorum* were fractionated into n-butanol fraction, ethyl acetate fraction, and crude extract to assess their oral antiulcer efficacy. Ethyl acetate fraction significantly attenuated acetic acid-induced oral ulcers in rats, reducing TNF-α and IL-2 levels, and markedly up-regulating proliferating cell nuclear antigen (PCNA) expression, indicative of enhanced mucosal regeneration. Crude extract and n-butanol fraction demonstrated comparatively modest effects (25) (Table 2).

The efficacy of the methanolic extract of *A. maurorum* was compared to that of albendazole in a controlled murine model of trichinellosis. Following oral administration of larvae to mice, infected groups received either albendazole or Alhagi extract, while corresponding controls remained untreated or uninfected. Parasitological evaluation revealed a marked reduction in both intestinal adult worms and muscle-stage larvae in the Alhagi-treated group compared to untreated infected mice. Treatment with *A. maurorum* resulted in significant down-regulation of pro-inflammatory cytokines (interferon-gamma (IFN-γ), TNF-α, transforming growth factor-beta (TGF-β), IL-2, IL-4, IL-12) and a concurrent increase in the anti-inflammatory mediator IL-10 (83).

The ethanolic extract of *A. maurorum* demonstrated pronounced anti-inflammatory activity in the context of immune-mediated hepatitis. *A. maurorum* extract administration significantly suppressed serum levels of key pro-inflammatory cytokines, including TNF-α and IL-6. Histological analyses revealed marked attenuation of inflammatory infiltration and necrotic lesions in hepatic tissue (56).

Renal system

A. maurorum exerted anti-inflammatory effects by down-regulating pro-inflammatory signaling pathways activated by lead exposure. Treated rats exhibited reduced protein expression of IL-6, TNF-α, and cyclooxygenase-2 (COX-2) in renal tissues (67).

Systemic inflammation

Treating Hu lambs with Alhagi honey–derived small-molecule sugars at high dose exerted measurable anti-inflammatory effects. Cytokine profiling revealed a favorable shift marked by up-regulation of IL-4, IL-10, and IL-17,

Table 2. Summary of anti-inflammatory and immunoregulatory properties of *Alhagi maurorum* in experimental models

Compound	Study design	Doses/Duration	Results	Ref.
		Anti-inflammatory effects		
		In vivo		
Camelthorn fractions	acetic acid-induced oral ulcers in rats	2 drop topical gel (5% fractions), 14 days	↑ PCNA expression ↓ TNF-α, IL-2	(25)
CME	*Trichinella spiralis* infected mice	400 mg/kg, 35 days, PO.	↑ IL-10 ↓ IFN-γ, TNF-α, TGF-β, IL-2, IL-4, IL-12	(83)
CEE	Concanavalin A-induced hepatitis in mice	300 mg/kg, 5 days, PO	↓ TNF-α and IL-6, inflammatory infiltration and necrotic lesions	(56)
CME	Lead-induced nephrotoxicity in rats	100, 200 mg/kg, 28 days, PO	↓ pro-inflammatory signaling, IL-6, TNF-α, and COX-2 renal expression	(67)
CH	Administration of CH to Hu lambs	200, 400, 800 mg/kg, 28 days, PO	↑ IL-4, IL-10, IL-17, expression of TNF-α in serum	(72)
		Immunomodulatory effects		
		In vitro		
CH	human Caco-2 epithelial and dendritic cells	-	↑ pIgR expression in Caco-2 cells, of immunoregulatory cytokine secretion in dendritic cells	(85)
		In vivo		
CHP	Administration of CHP to mice	200, 400, 800 mg/kg, 7 days, IG	↑ sIgA, β-defensins, mucosal immunity, lymphocyte counts, IgA^+ cells, IL-2, IL-4, IL-6, IL-10, IL-17, IFN-γ, TNF-α, $CD3^+$, $CD4^+$, $CD8^+$ T-cell	(87)
CHP	Cyclophosphamide-induced immunosuppressed mice	800 mg/kg, 7 days, PO	↑ CCL20 expression, $CD4^+$, $CD8^+$ T lymphocytes, and B cells activation and expansion, sIgA, pIgR, J-chain, IgA^+ cell populations	(85)
CEE	Concanavalin A-induced hepatitis in mice	300 mg/kg, 5 days, PO	↓ hepatic $CD4^+$ T cell infiltration, IFN-γ expression	(56)
CH	Administration of CH to Hu lambs	200, 400, 800 mg/kg, 28 days, PO	↑IgA, IgG, IgM levels, IFN-γ expression	(72)

CD: cluster of differentiation; CEE: camelthorn ethanolic extract; CH: camelthorn honey; CHP: camelthorn honey polysaccharides; CME: camelthorn methanolic extract; COX-2: cyclooxygenase-2; i.g.: intragastric; IFN-γ: interferon-gamma; Ig: immunoglobulin A; IL: interleukin; p.o.: per os (oral administration); PCNA: proliferating cell nuclear antigen; pIgR: polymeric immunoglobulin receptor; sIgA: secretory immunoglobulin A; TGF-β: transforming growth factor beta; TNF-α: tumor necrosis factor alpha

alongside increased expression of TNF-α in serum (72).

Table 2 presents a consolidated overview of the anti-inflammatory effects of *A. maurorum*, indicating its effects on inflammatory mediators in different experimental models.

The aggregate of *in vivo* investigations highlights the compelling anti-inflammatory capacity of Alhagi, across gastrointestinal, hepatic, renal, and systemic contexts. Mechanistically, the extracts consistently attenuate key pro-inflammatory mediators (Figure 1), including TNF-α, IL-1β, IL-6, and IFN-γ, while preserving or enhancing regulatory cytokines such as IL-10 and IL-4. This immunomodulatory profile reflects not only suppression of cytokine synthesis but also interference with upstream signaling pathways, such as NF-κB and COX-2, which are instrumental in propagating tissue-specific inflammation.

Beyond cytokine modulation, several studies report structural and functional restoration of damaged tissues. Up-regulation of PCNA, for instance, implies proliferative and regenerative effects within ulcerated mucosa, while histological analyses in hepatic and renal models consistently demonstrate reduced leukocytic infiltration and necrotic foci. These findings suggest that the therapeutic value of Alhagi may extend beyond immune regulation to encompass cytoprotective, wound-healing, and epithelial-repair functions-hallmarks of a compound class capable of restoring organ integrity under inflammatory stress. Such dual activity reinforces the translational potential of Alhagi-derived treatments, especially where chronic inflammation coexists with degenerative pathology.

However, several methodological shortcomings must be acknowledged. Many studies used short intervention windows, limited dose ranges, and failed to justify selected concentrations with pharmacokinetic data or bioavailability profiling. The absence of standardization in extract preparation, ranging from crude hydroalcoholic formulations to semi-purified fractions, introduces variability that complicates comparative analysis. Moreover, functional endpoints such as organ-specific performance or behavioral correlates were largely absent, which limits our understanding of systemic efficacy and safety. Few studies incorporated rigorous experimental controls, such as sham-treated or placebo groups, nor did they address potential confounders such as environmental exposures or microbiota interactions.

Interestingly, one contradictory finding emerged from serum cytokine studies in Hu lambs, where TNF-α was paradoxically elevated despite concurrent rises in IL-4, IL-10, and IL-17. This may reflect a species-specific immunological response or the unique pharmacodynamics of Alhagi-derived sugars compared with whole-plant extracts. Alternatively, it could suggest biphasic dose-dependent effects, with low and high concentrations triggering differential immune pathways, a hypothesis warranting further exploration through dose-ranging and time-course experiments.

Translating these findings into clinical practice demands a rigorous roadmap. Standardization of active constituents through metabolomic profiling, combined with scalable formulation strategies such as phospholipid encapsulation, could enhance reproducibility and bioavailability. Moreover, testing across autoimmune and metabolic models may elucidate conserved mechanistic targets, enabling broader therapeutic deployment. While the current evidence base positions Alhagi species as promising anti-inflammatory agents, only through meticulous optimization and mechanistically guided clinical trials can their full therapeutic potential be realized.

Immunomodulatory effects

The immune system defends the body against both internal disruptions and external threats through a complex interplay between its innate and adaptive branches. Innate immunity is facilitated by cellular components such as natural killer cells and phagocytic leukocytes, including macrophages, monocytes, and neutrophils, which act swiftly

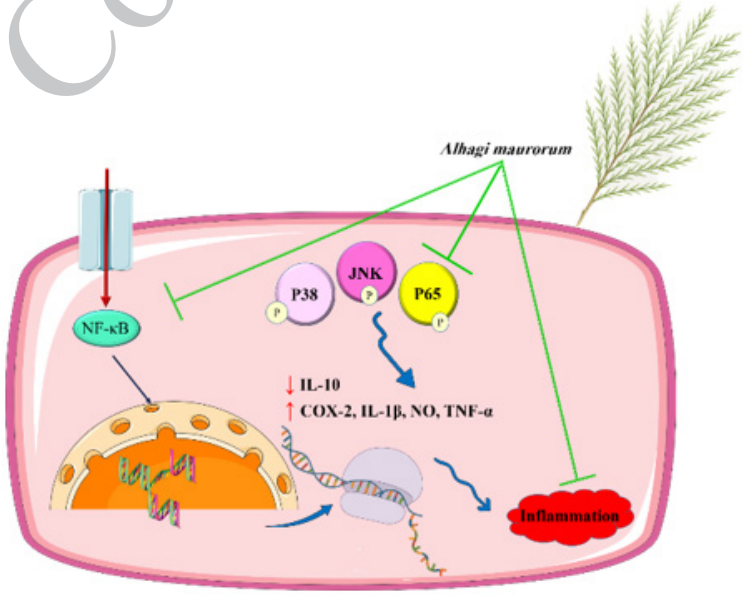

Figure 1. Schematic representation of the anti-inflammatory effects of *Alhagi maurorum* through modulation of cellular signaling pathways
The plant inhibits activation of the NF-κB pathway, resulting in reduced phosphorylation of P38, JNK, and P65—key intermediates in pro-inflammatory signaling. Consequently, the transcription and expression of inflammatory mediators, including COX-2, IL-1β, NO, and TNF-α, are down-regulated, while IL-10 expression is up-regulated, promoting an anti-inflammatory cellular phenotype (Images from https://smart.servier.com).

to neutralize harmful agents. In contrast, adaptive immunity generates antigen-specific memory cells following initial exposure to allergens, thereby intensifying and refining the immune response upon subsequent encounters (20, 84). In this context, *A. maurorum* has emerged as a botanical with demonstrable immunomodulatory activity across various inflammatory and autoimmune conditions, suggesting its potential as a therapeutic agent for immune-related pathologies.

In vitro

Epithelial and dendritic cells

Experiments conducted on human Caco-2 epithelial cells and dendritic cells revealed that Alhagi honey polysaccharide exerts pronounced immunostimulatory effects at the cellular level. Treatment with Alhagi honey polysaccharide significantly up-regulated expression of polymeric immunoglobulin receptor (pIgR) in Caco-2 cells, which is critical for transcytosis and mucosal immunoglobulin (Ig)A transport. In dendritic cells, Alhagi honey polysaccharide promoted maturation and induced the secretion of immunoregulatory cytokines, indicating its capacity to modulate antigen-presenting cell behavior and shape downstream immune responses (85).

T cells

To explore the immunomodulatory potential of Taranjebin manna derived from *Poophilus nebulosus* Leth. larvae feeding on *A. maurorum*, a study evaluated both the crude aqueous extract and its high-molecular-weight fractions on Jurkat E6.1 human T cells. It was found that while the unprocessed solution stimulated cellular proliferation, three of four purified acidic polysaccharides markedly suppressed proliferation in a dose-dependent manner (86).

In vivo

Digestive system

Alhagi honey polysaccharides demonstrated significant immunomodulatory and microbiota-enhancing effects in a short-term murine study. Daily intra-gastric administration of Alhagi honey led to marked improvements in intestinal barrier integrity, evidenced by elevated levels of secretory IgA (sIgA) and β-defensins. Enhanced mucosal immunity was further reflected by increased intraepithelial lymphocyte counts, higher proportions of IgA$^+$ cells in the lamina propria, and robust up-regulation of cytokines including IL-2, IL-4, IL-6, IL-10, IL-17, IFN-γ, and TNF-α. Lymphocyte profiling revealed significant expansion of cluster of differentiation (CD)3$^+$, CD4$^+$, and CD8$^+$ T-cell subsets in both mesenteric lymph nodes and Peyer's patches. Meanwhile, 16S ribosomal DNA (rDNA) sequencing of fecal samples indicated a richer and more diverse microbial composition, characterized by increased probiotic abundance and reduced levels of pathogenic species (87).

Following cyclophosphamide-triggered immune suppression in a murine model, oral administration of Alhagi honey polysaccharide restored intestinal immune function through multiple synergistic pathways. Alhagi honey polysaccharide enhanced dendritic cell maturation and increased expression of chemokine C-C motif ligand 20 (CCL20), thereby facilitating recruitment of additional DCs to intestinal sites. This cascade led to the activation and expansion of CD4$^+$ and CD8$^+$ T lymphocytes as well as B cells. Further immunophenotyping indicated increased differentiation of T helper cells and elevated sIgA levels, supported by up-regulation of pIgR, J-chain, and IgA$^+$ cell populations in intestinal tissues. Additionally, Alhagi honey polysaccharide promoted the production of short-chain fatty acids in the cecum, which are known to influence mucosal barrier integrity and immune regulation (85).

A. maurorum ethanolic extract demonstrated potent immunomodulatory properties in mice challenged with concanavalin A. A pronounced reduction in hepatic CD4$^+$ T cell infiltration was observed, along with decreased expression of IFN-γ (56).

In a comparative study evaluating the immunomodulatory potential of *A. maurorum* polysaccharides derived from two distinct regions in Xinjiang, China-Shanshan (SS) and Aksu (AK)-researchers found that the SS-derived polysaccharides, particularly those harvested at the plant's maturity stage, exhibited superior immunoenhancing effects in lambs. Lambs treated with SS polysaccharides showed significant improvements in intestinal immune parameters, including elevated levels of IgA in the duodenum, jejunum, and ileum, as well as increased serum IgG and cytokines such as IL-4, IL-10, IL-17, and TNF-α. Morphological enhancements in intestinal architecture, such as increased villus height and crypt depth, were also observed. Moreover, SS polysaccharides activated B-cell receptor signaling and IgA production pathways via the T-dependent route, thereby promoting mucosal immunity (88).

Systemic immune dysregulation

To overcome the limited bioavailability of Alhagi honey polysaccharide despite its potent immunoadjuvant properties, researchers developed a nanoparticle-based delivery system using poly(lactic-co-glycolic acid) (PLGA) modified with cationic polymers. Three distinct cationic coatings were applied to Alhagi honey polysaccharide-loaded PLGA nanoparticles, generating positively charged carriers optimized for antigen delivery. Among these, the polyethyleneimine-coated formulation encapsulating H5N1 antigen demonstrated superior immunogenicity in murine models. Mice were immunized with polyethyleneimine-Alhagi honey polysaccharide-loaded PLGA nanoparticles, which exhibited elevated hemagglutination inhibition titers, enhanced IgG subtypes, and robust cytokine responses. Immunophenotyping revealed activation of dendritic cells in lymph nodes and increased populations of CD4$^+$ and CD8$^+$ T cells in the spleen. Polyethyleneimine-Alhagi honey polysaccharide-loaded PLGA nanoparticles promoted high expression of major histocompatibility complex class (MHC) I and II molecules on dendritic cells, facilitated sustained antigen release at the injection site, and achieved targeted delivery to lymphoid tissues (82).

Investigating the immunomodulatory potential of Alhagi honey-derived polysaccharides, formulated into PLGA-based Pickering emulsions, specifically PLGA polysaccharide assembled system (PPAS) and its polyethyleneimine-modified variant, polyethyleneimine-PPAS, demonstrated high loading efficiency and sustained release of ovalbumin as a model antigen. *In vivo* evaluations revealed that polyethyleneimine-PPAS/ovalbumin markedly enhanced IgG production and elevated cytokine levels, indicating robust immune activation. Notably, this formulation effectively targeted dendritic cells, facilitated antigen uptake, and promoted dendritic cell maturation within lymph

nodes. Mechanistically, the immunostimulatory effects appeared to involve both MHC class I and II pathways (89).

High-dose Alhagi honey–derived small-molecule sugar supplementation improved immunological competency in Hu lambs. Circulating levels of IgA, IgG, and IgM were significantly increased. It also increased expression of IFN-γ (72). Table 2 summarizes diverse experimental findings on *A. maurorum*, underscoring its immunoregulatory properties observed across multiple biological models.

In summary, *A. maurorum* and its bioactive derivatives-including honey polysaccharides, ethanolic extracts, small-molecule sugars, and Taranjebin manna-exhibit a multidimensional profile of immunomodulatory activity, driven primarily by their capacity to engage mucosal immune signaling and enhance both innate and adaptive responses (Figure 2). Collectively, these compounds activate epithelial transcytosis pathways (notably via pIgR and J-chain up-regulation), stimulate dendritic cell maturation, and modulate cytokine profiles across intestinal, hepatic, and systemic compartments. The induction of pIgR-mediated IgA transport, B-cell receptor signaling, and T-helper cell differentiation suggests that Alhagi-derived compounds interact with pattern recognition receptors such as TLRs and CCL20-mediated chemokine cascades, ultimately amplifying mucosal barrier integrity and immunosurveillance. Markedly, the restoration of immune parameters in cyclophosphamide-induced models and the enhancement of short-chain fatty acid biosynthesis underscore the therapeutic promise in immunocompromised or dysbiotic states.

A key novelty that emerges from synthesizing these findings is the context-dependent duality of Alhagi's immune effects. While crude Taranjebin exhibited lymphoproliferative properties, its purified acidic polysaccharides reversed this trend and demonstrated inhibitory activity-hinting at selective regulation depending on molecular fraction, dose, and immune status. This biphasic behavior could be strategically coupled in immunotherapeutic design, allowing for targeted modulation depending on inflammatory load or disease phase. Nonetheless, the interpretive potential of these findings is constrained by methodological inconsistencies-such as dosage heterogeneity, limited mechanistic resolution, and the absence of standardized immunological benchmarks-which warrant cautious consideration before translational extrapolation. For instance, many studies employ high or non-physiological dosages, lack rigorous dose-response modeling, and fail to use standardized antigenic or stressor controls, complicating translational extrapolation. Moreover, divergent species and cell line models-from Caco-2 cells to Hu lambs-present challenges in defining human-relevant pharmacodynamics.

The use of advanced delivery platforms, such as PLGA-nanoparticle encapsulation, addresses the intrinsic bioavailability limitations of Alhagi and opens new avenues for vaccine adjuvant applications. Yet, direct comparisons between molecular forms (e.g., small sugars vs acidic polysaccharides) and across environmental sources (e.g., Shanshan vs Aksu) remain underexplored. Incorporating omics-based profiling and standardized immunophenotyping protocols could better explain active constituents and inform dosing thresholds. Contradictions across models-particularly between the immunostimulatory actions in epithelial/dendritic cells and the suppressive effects seen in T cells-are likely attributable to differential receptor expression, tissue microenvironment, and temporal dynamics of immune activation. Future efforts should aim to stratify the effects of Alhagi by immune context and formulation type to refine its role in personalized immunotherapy or as an ethnobotanical vaccine enhancer.

Anti-apoptotic effects

Apoptosis, a finely regulated mechanism of programmed cell death, plays a critical role in maintaining cellular

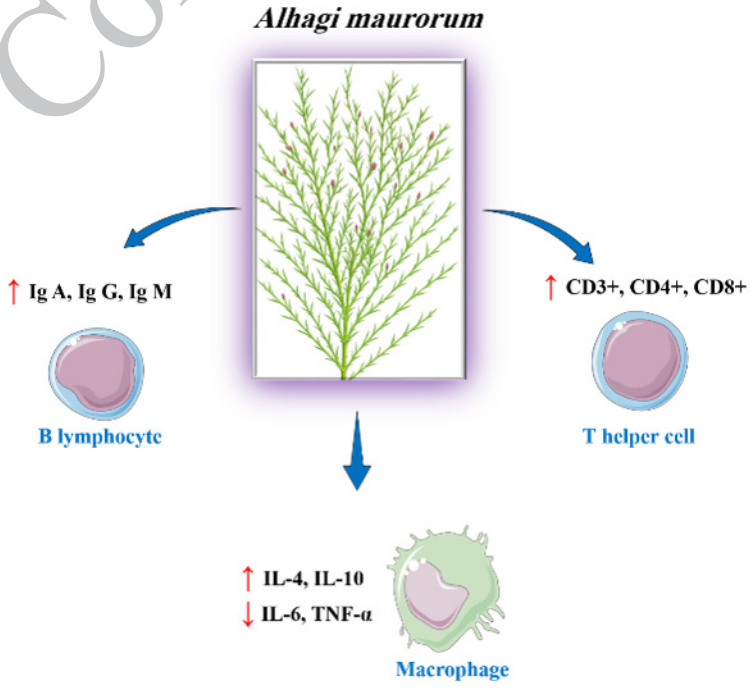

Figure 2. Immunomodulatory interactions between *Alhagi maurorum* and key immune cell populations
The diagram illustrates the proposed effects of the plant on B lymphocytes, T helper cells, and macrophages (images from https://smart.servier.com).

equilibrium and tissue integrity. This physiological process is typically initiated in response to cellular injury, environmental stressors, or specific molecular cues (90). Its disruption, whether through excessive activation or insufficient clearance, has been implicated in a broad spectrum of pathologies affecting vital organs, including the heart (91), liver (92), kidneys (93), and brain (94). Central to apoptotic regulation are molecular mediators such as caspase enzymes and B-cell lymphoma 2 (Bcl-2) protein family members (95), whose arrangement of signaling cascades, especially through the mitochondrial and death receptor pathways, ensures the precise execution of cell death in response to varying stimuli. When these regulatory networks are compromised, the resulting imbalance may permit the persistence of damaged cells or trigger premature cell loss, both of which contribute to disease progression (96).

Advancing our understanding of apoptosis-related molecular dynamics is therefore essential to identifying therapeutic targets, particularly in diseases underpinned by atypical cell death. Emerging investigations into natural bioactive compounds such as those found in *A. maurorum offer* captivating prospects for modulating apoptotic pathways. Their potential anti-apoptotic effects warrant deeper mechanistic analysis and could inform novel strategies aimed at restoring tissue health and mitigating apoptosis-associated disorders.

In vivo

Digestive system

A. maurorum ethanolic extract exerted notable anti-apoptotic effects in the context of concanavalin A-induced hepatitis. Treated mice exhibited significant down-regulation of pro-apoptotic markers, including Bcl-2-associated X protein (Bax) and caspase-3, alongside suppression of JNK activity. Concurrently, the extract enhanced the expression of Bcl-2. Histopathological examination corroborated these molecular findings, revealing diminished hepatocyte necrosis and preserved tissue architecture (56) (Table 3).

Endocrine system

Researchers evaluated the influence of *A. maurorum* alcoholic extract on hepatic caspase-3 gene expression in streptozotocin-induced diabetic rats. The study involved six groups, including healthy controls, diabetic controls, and extract-treated animals at two different doses, administered either alone or following streptozotocin injection. A significant elevation of caspase-3 expression was observed in diabetic rats compared to controls. However, rats receiving *A. maurorum* extract post-induction exhibited a dose-dependent attenuation in gene expression (97).

Renal system

Lead exposure triggered up-regulation of the pro-apoptotic gene Bax and down-regulation of the anti-apoptotic gene Bcl-2 in renal tissue of rats. Co-administration of *A. maurorum* reversed this expression pattern, promoting cell survival (67).

In brief, the compiled evidence strongly supports the anti-apoptotic potential of *A. maurorum* alcoholic extract across distinct pathological contexts, particularly within hepatic and renal systems. The protective mechanism appears to involve modulation of intrinsic apoptotic signaling, including suppression of pro-apoptotic mediators such as caspase-3 and Bax, and enhancement of anti-apoptotic factors like Bcl-2 (Figure 2). Additionally, attenuation of upstream regulators-such as JNK-suggests that the extract exerts its effects not only at the execution phase of apoptosis but also at pivotal stress-sensing checkpoints. This multi-targeted action likely stems from the extract's rich reservoir of polyphenolic anti-oxidants, including flavonoids and anthocyanins, which are known to inhibit oxidative stress-induced apoptotic cascades and preserve mitochondrial integrity.

These findings have compelling translational implications: by targeting apoptotic pathways implicated in diabetic hepatopathy, chemical nephrotoxicity, and immune-mediated hepatitis, *A. maurorum* may represent a promising adjunct to conventional therapies aimed at

Table 3. Summary of anti-apoptotic and anti-cancer properties of *Alhagi maurorum* in experimental models

Compound	Study design	Doses/Duration	Results	Ref.
		Anti-apoptotic effects		
		In vivo		
CEE	Concanavalin A-induced hepatitis in mice	300 mg/kg, 5 days PO	↑ Bcl-2 expression ↓ Bax, caspase-3, JNK activity, hepatocyte necrosis	(56)
CEE	Streptozotocin-induced diabetic rats	250, 500 mg/kg	↓ hepatic caspase-3 gene expression, apoptosis	(97)
CME	Lead-induced nephrotoxicity in rats	100, 200 mg/kg, 28 days, PO	↑ Bcl-2 in renal tissue, cell survival ↓Bax	(67)
		Anti-cancer effects		
		In vitro		
CAE titanium nanoparticles	Human breast cancer cell lines	0-1000 µg/ml	↓ cell viability	(102)
CHAE	4T1 cells	15, 31, 51, 62, 125 µg/ml	↑ apoptosis ↓ cell growth and motility, HIF1-α, FZD7	(103)
CME of the aerial parts	HL-60 cells	10, 50, 100 µg/ml	↑ radical scavenging activity, antiproliferative effects	(107)
Camelthorn seed AE zinc oxide nanoparticles	Osteosarcoma and HUVEC cell lines	0-1000 µg/ml	↑ antitumor efficacy, antioxidant capacity	(108)
		In vivo		
CHAE	Mice with breast cancer	500, 10000 mg/kg, 3 weeks, IP	↓ tumor growth and size, β-catenin, FZD7, HIF1-α, MMP2, VEGF A	(110)

Bax: bcl-2-associated x protein; Bcl-2: b-cell lymphoma 2; CAE: camelthorn aqueous extract; CEE: Camelthorn ethanolic extract; CHAE: Camelthorn hydro-alcoholic extract; CME: Camelthorn methanolic extract; FZD7: frizzled class receptor 7; HIF1-α: hypoxia-inducible factor 1 subunit alpha; i.p.: intraperitoneal; JNK: c-jun n-terminal kinase; MMP2: matrix metallopeptidase 2; p.o.: per os (oral administration); Ref: reference; VEGF: vascular endothelial growth factor; AE: aqueous extract

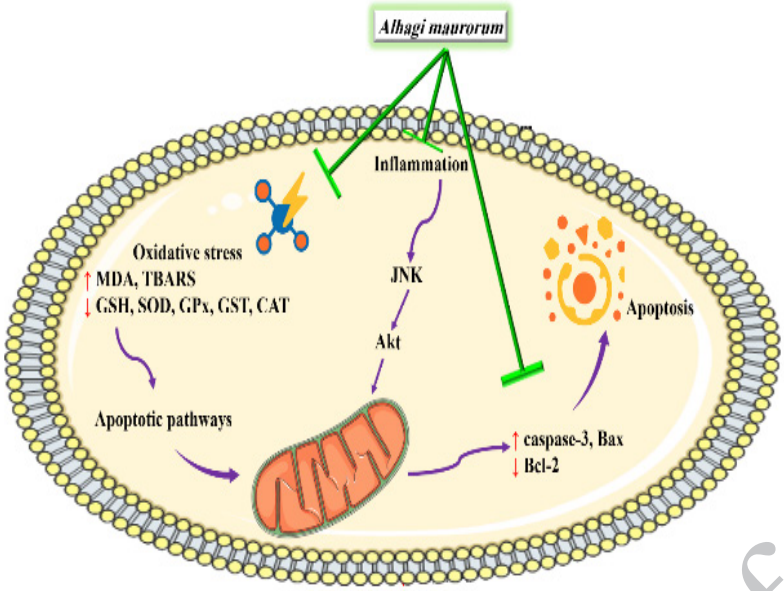

Figure 3. Illustration of cellular protective mechanisms mediated by *Alhagi maurorum* against oxidative stress, inflammation, and apoptosis
The extract enhances antioxidant defense by up-regulating enzymes such as GSH, SOD, GPx, GST, and CAT while reducing lipid peroxidation markers (MDA, TBARS). Simultaneously, it attenuates inflammatory signaling (via JNK and Akt pathways) and suppresses apoptosis through down-regulation of caspase-3 and Bax and up-regulation of Bcl-2, contributing to mitochondrial integrity and overall cytoprotection (Images from https://smart.servier.com)
GSH: glutathione; SOD: superoxide dismutase; GPx: glutathione peroxidase; GST: glutathione S-transferase; CAT: catalase

mitigating organ damage. However, several methodological limitations temper this enthusiasm. Dosing strategies varied across studies, with insufficient justification for selected concentrations and a lack of pharmacokinetic profiling to confirm bioavailability or systemic exposure. Moreover, while most experiments used appropriate controls, the absence of vehicle-only groups in certain designs obscures whether observed effects stem from the active components of the extract or nonspecific solvent interactions. The reliance on male rodents also limits generalizability, as sex-specific apoptotic responses may differ.

Strengths of the current body of research include consistent dose-dependent molecular and histological outcomes across diverse models, reinforcing the biological relevance of *A. maurorum*. To bridge preclinical promise with clinical application, future studies must address pharmacodynamic endpoints, long-term safety, and potential herb-drug interactions. Developing standardized extract formulations and incorporating disease-relevant biomarkers would further enhance translational credibility. Ultimately, the convergence of anti-oxidant and anti-apoptotic properties in *A. maurorum* positions it as a candidate for integrative therapy, especially in metabolic and inflammatory disorders where apoptotic dysregulation contributes to organ compromise.

Anti-cancer effects

Cancer is a multifaceted disease characterized by uncontrolled cell proliferation, evasion of apoptosis, sustained angiogenesis, and the potential for metastasis, resulting in significant morbidity and mortality worldwide (98, 99). Its pathogenesis involves a complex interplay of dysregulated inflammatory responses, epigenetic alterations, genetic mutations, and oxidative stress that disrupt normal tissue architecture and cellular signaling (100). Conventional therapeutic modalities, such as chemotherapy, radiotherapy, and targeted immunotherapy, have achieved substantial advances, yet their efficacy is often limited by drug resistance, systemic toxicity, and tumor heterogeneity (101).

In this context, phytochemicals from medicinal plants have attracted growing interest due to their multi-targeted mechanisms and favorable safety profiles. *A. maurorum* has emerged as a promising botanical candidate, demonstrating anticancer activity through anti-oxidant regulation, induction of cell-cycle arrest, apoptosis promotion, and suppression of tumor-associated inflammation and angiogenesis. The next section will delve into the anti-cancer potential of *A. maurorum*, exploring its bioactive constituents and molecular mechanisms of action across various cancer models.

In vitro

Breast cancer cells

Titanium nanoparticles were biosynthesized using *A. maurorum* extract in an aqueous medium, serving as both a reducing and stabilizing agent. The cytotoxic potential of titanium nanoparticles was assessed against four human breast cancer cell lines. Results demonstrated a dose-dependent decrease in cell viability, with titanium nanoparticles showing significantly lower half-maximal inhibitory concentration (IC_{50}) values compared to the crude *A. maurorum* extract across all cell lines, most notably in Hs 319.T cells (102).

Evaluating the anticancer efficacy of *A. maurorum* extract, individually and in combination with docetaxel, against 4T1 breast cancer cells indicated that the extract inhibited cell growth. Co-treatment experiments revealed that *A. maurorum* acted synergistically with docetaxel. Migration assays indicated that the extract, alone or combined with docetaxel, suppressed the motility of 4T1 cells. Apoptosis was evident in the combination treatments. Molecular profiling showed that *A. maurorum* plus docetaxel down-regulated hypoxia-inducible factor 1-subunit alpha

(HIF1-α) and frizzled class receptor 7 (FZD7) (103).

Furthermore, cerium oxide nanoparticles were synthesized via a green protocol using *A. maurorum* extract as a biologically active reducing and stabilizing agent. Biological assessments demonstrated that cerium oxide nanoparticles exerted concentration-dependent cytotoxic effects against breast cancer cell lines (104).

Lung cancer cells

Hydroalcoholic extract of *A. maurorum* has shown potential anticancer activity against non-small-cell lung cancer. Pathway analyses identified PI3K/Akt signaling as a key pathway involved in the disease. In A549 lung cancer cells, the extract exhibited cytotoxic activity with an IC_{50} of 277 µg/ml and also showed dose-dependent anti-oxidant effects. Further analysis indicated modulation of PI3K/Akt-related gene expression (105).

Gastric carcinoma cell

Gold nanoparticles were synthesized via a green chemistry approach using aqueous leaf extract of *A. maurorum* as a natural reducing and stabilizing agent. The cytotoxic effects of gold nanoparticles were evaluated against several gastric carcinoma cell lines as well as normal endothelial cells (HUVEC). Gold nanoparticles reduced cancer cell viability in a dose-dependent manner, showing strongest activity against MKN45 cells (33).

Liver cancer cells

In an *in vitro* study, the findings highlight the anticancer potential of select secondary metabolites from *A. maurorum* against liver cancer cell lines. After pharmacophore-based screening, eight compounds were identified as active, and subsequent molecular docking studies revealed their capacity to interact with protein targets relevant to hepatocellular carcinoma (HCC) and HepG2 cells. Among these, compound F52 exhibited the highest predicted binding affinity and emerged as the most promising candidate (106).

Human leukemia cells

In a pharmacological evaluation, methanolic extracts from the aerial parts of *A. maurorum* were investigated for their bio-functional properties. Leaf extracts showed superior radical scavenging activity. Cytotoxicity analyses on HL-60 human leukemia cells indicated significant anti-proliferative effects, with IC_{50} values of 16.0 µg/ml for leaf extracts and 22.0 µg/ml for flower extracts (107).

Osteosarcoma cells

In this experimental investigation, zinc oxide nanoparticles (ZnONPs) were biosynthesized in an aqueous medium using *A. maurorum* seed extract, serving as both reducing and stabilizing agents. The ZnONPs exhibited dose-dependent antitumor efficacy against osteosarcoma cells while sparing normal endothelial cells, suggesting selective cytotoxicity. Additionally, radical scavenging assays demonstrated notable anti-oxidant capacity, comparable to butylated hydroxytoluene (108).

Prostate carcinoma cells

In a study, gold nanoparticles were biosynthesized via a green methodology utilizing the aqueous leaf extract of *A. maurorum*. Their anticancer activity was evaluated *in vitro* on prostate carcinoma cell lines alongside HUVEC. Gold nanoparticles elicited a dose-dependent cytotoxic response across the carcinoma lines. Furthermore, gold nanoparticles demonstrated appreciable activity, although lower than the synthetic anti-oxidant butylated hydroxytoluene (109).

In vivo

Breast

In a preclinical investigation targeting metastatic breast cancer, *A. maurorum*, both alone and in combination with docetaxel, was evaluated for its tumor-suppressive efficacy in 4T1 cell-bearing mice. Intraperitoneal administration of *A. maurorum* and docetaxel markedly reduced tumor burden, with the combination therapy yielding the most pronounced inhibition in tumor growth and size. Molecular analyses via RT-PCR revealed down-regulation of key oncogenic and angiogenic mediators including β-catenin, FZD7, HIF1-α, matrix metallopeptidase 2 (MMP2), and vascular endothelial growth factor (VEGF), particularly in the co-treatment group. This was accompanied by favorable shifts in biochemical parameters such as serum ALT and urea, supporting improved systemic tolerance (110).

In Table 3, a synthesis of preclinical data illustrates the anti-cancer potential of *A. maurorum* in varied study contexts.

The anticancer activity of *A. maurorum* is verified through a range of *in vitro* and *in vivo* investigations, collectively pointing to its multifaceted therapeutic promise. Rather than isolated outcomes, the results converge to highlight a consistent pattern of selective cytotoxicity, particularly when *A. maurorum* is employed either as a crude extract or as a biosynthetic agent for metal-based nanoparticles. Its ability to inhibit cancer cell proliferation, trigger apoptosis, and impede metastatic signaling appears to exceed specific cancer types spanning breast, gastric, liver, prostate, leukemia, and osteosarcoma models.

Mechanistically, *A. maurorum* intervenes in cancer progression through several complementary routes. One central feature is its modulation of apoptosis-related genes, with down-regulation of anti-survival markers such as Bcl-2 and HIF1-α and up-regulation of pro-apoptotic players like Bax and caspase-3. In addition, it targets migratory and angiogenic pathways by attenuating FZD7, β-catenin, VEGF-A, and MMP2, offering a compelling strategy to limit tumor spread. Particularly, the green synthesis of nanoparticles using its extract adds not only biochemical potency but also ecological and pharmacological advantages, indicating its dual role as a therapeutic agent and a biogenic carrier system.

Still, despite the strong preclinical signals, methodological inconsistencies temper the strength of these findings. Dose determination and standardization remain problematic, with IC_{50} values exhibiting substantial variation due to differences in cell lines, extract preparation, and nanoparticle characteristics. Experimental controls are inconsistently reported, particularly in studies comparing crude extracts to nanoparticle formulations, which makes it difficult to isolate the true contribution of *A. maurorum*. Most *in vitro* studies lack long-term exposure models or assessments of cellular adaptive responses, leaving open questions about the durability of its anticancer effects. Moreover, while some studies indicate synergy with established chemotherapeutics like docetaxel, others offer conflicting profiles regarding gene regulation and cytotoxic thresholds, raising concerns

about reproducibility and context-dependence.

In vivo studies, though relatively limited in scope, provide encouraging evidence of tumor suppression and systemic tolerance, especially in breast cancer models. The documented reductions in tumor volume, alongside favorable modulation of hepatic and renal biomarkers, suggest potential for integration into combination therapies. However, translational progression remains constrained by the absence of pharmacokinetic profiling, immunomodulatory analyses, and toxicity studies. Without these critical data points, the jump from laboratory efficacy to clinical utility cannot yet be fully justified.

To move beyond proof-of-concept, future research must prioritize mechanistic clarity and experimental rigor. Standardizing extract composition, defining active constituents, and validating therapeutic targets through molecular docking and multi-omics platforms will be essential. Moreover, exploring its role in modulating the tumor microenvironment, especially immune surveillance and oxidative stress adaptation, could unlock new translational pathways.

Taken as a whole, *A. maurorum* stands out not merely for its ethnopharmacological heritage but for its potential as a source of novel oncologic agents. Its effectiveness across cancer models, coupled with its biocompatibility in nanoparticle systems, points toward a valuable role in integrative cancer therapeutics provided that methodological refinements and mechanistic studies evolve together.

Future perspectives

Building upon the emerging therapeutic profile of *A. maurorum*, future research should aim to transform its ethnopharmacological legacy into clinically actionable interventions. Although preclinical data suggest promising anti-oxidant, anti-inflammatory, anti-apoptotic, anticancer, and immunomodulatory activities, systematic investigations into its pharmacokinetics, bioavailability, metabolic fate, and organ-specific toxicity remain notably absent. Addressing these gaps will be essential for transitioning from descriptive efficacy to evidence-based formulation design.

Advancements in nanotechnology offer a parallel frontier for optimizing the therapeutic value of *A. maurorum*. Its capacity to biosynthesize metal-based nanoparticles introduces an ecological and pharmacodynamic advantage, yet the variability in nanoparticle size, surface charge, and release kinetics demands standardization. Future studies should integrate multi-omics platforms transcriptomics, proteomics, and metabolomics to elucidate its molecular targets and identify compound-specific pathways that mediate its therapeutic effects. Such data may inform the development of targeted delivery systems and combinatorial regimens, especially in oncology and immunotherapy.

From a clinical translation perspective, randomized controlled trials and phase I safety studies are critical next steps. Moreover, *A. maurorum*'s role in modulating immune homeostasis and inflammatory cascades may be relevant to autoimmune disorders, chronic metabolic syndromes, and mucosal immunity applications that remain largely unexplored. Interdisciplinary collaborations among pharmacologists, materials scientists, and clinicians will be pivotal in repositioning A. maurorum from a botanical adjunct to a centerpiece of integrative medicine. Ultimately, its therapeutic horizons may extend not only through its constituent phytochemicals but also through its narrative as a botanical bridge between tradition and translational innovation.

Limitations and risk of bias

In the present article, anti-oxidant, anti-inflammatory, anti-apoptotic, anticancer, and immunomodulatory effects of *A. maurorum* were reviewed. These biological activities were selected because they represent the most consistently documented and pharmacologically relevant mechanisms associated with a wide range of diseases, and they are supported by the most substantial body of evidence currently available for *A. maurorum*. Moreover, to preserve the manuscript's focus and depth within practical word and reference limits, we intentionally concentrated on these core mechanisms rather than expanding the scope at the expense of critical discussion.

This narrative review has several limitations. First, substantial heterogeneity among studies, including differences in experimental models, plant parts, extraction methods, doses, and treatment durations, limits direct comparison and reproducibility. Second, publication bias may overstate efficacy, as positive findings are more commonly reported than negative results, toxicity data, or standardized therapeutic indices. Third, the frequent lack of blinding, inadequate reporting of limitations, and poor control of variables such as age, sex, and comorbidities reduce internal validity and translational relevance. Finally, because this is a narrative rather than a systematic or meta-analytic review, study selection may reflect implicit bias and lacks formal quality assessment. Future research should adopt more rigorous and transparent methodologies to define the therapeutic potential of A. maurorum better.

Conclusion

This narrative review positions *A. maurorum* as a typical botanical agent whose therapeutic spectrum spans anti-oxidant, anti-inflammatory, anti-apoptotic, anticancer, and immunomodulatory domains. Rooted in ethnomedicinal tradition yet increasingly validated by contemporary preclinical investigations, *A. maurorum* demonstrates how molecular complexity and contextual adaptability can merge into pharmacological relevance. Its bioactive constituents exert system-wide effects through mechanisms encompassing redox regulation, cytokine modulation, mitochondrial stabilization, apoptotic control, and immune system engagement.

Anti-oxidant effects are achieved via both direct scavenging of reactive oxygen species and transcriptional activation of endogenous defenses through Nrf2 and HO-1 pathways, supported by the enzymatic enhancement of SOD, CAT, GPx, and GSH. Anti-inflammatory effect stems from inhibition of pro-inflammatory signaling-particularly NF-κB and COX-2- and up-regulation of regulatory cytokines such as IL-4 and IL-10. Immunomodulatory properties center on mucosal and systemic immune architecture, with up-regulation of pIgR-mediated IgA transport, dendritic cell maturation, and T-helper cell polarization. The plant's anti-apoptotic potential is supported by modulation of caspase-3, Bax, Bcl-2, and upstream regulators like JNK, while its anticancer effects involve selective cytotoxicity, inhibition of angiogenic and migratory mediators such as VEGF A and MMP2, and biogenic nanoparticle synthesis that enhances delivery and ecological compatibility.

Beyond its molecular reach, the significance of A. maurorum lies in its symbolic and scientific capacity to bridge the conceptual gap between traditional medicine and evidence-based innovation. Its transdisciplinary potential as a therapeutic scaffold, a biotechnological resource, and a culturally embedded knowledge system marks it as more than a bioactive extract: it is a blueprint for integrative medicine. While methodological inconsistencies underscore the need for rigorous standardization, dose modeling, and clinical trials, the convergence of mechanistic depth, ecological sustainability, and therapeutic promise justifies elevating it from adjunct to protagonist in the evolving landscape of biomedical therapeutics.

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No new data were created or analyzed during this study. Data sharing does not apply to this article. All review papers are available through the corresponding author upon request.

Authors' Contributions

MH B rose the notion and supervised. M GR, M R, MR A, and HR E wrote the manuscript together. All authors approved the final version of the manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Declaration

During the preparation of this work, the author(s) used ChatGPT and QuillBot to rephrase and reduce plagiarism, and to improve language and grammar. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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