***Review Article***

**MULBERRY (MORUS SPP.): NATURE’S MEDICINE FOR MODERN HEALTH AND INDUSTRY**

**Abstract:**

Mulberry (Morus spp.), a plant long revered in traditional medicine, has emerged as a promising source of functional nutrients and pharmacologically active compounds. This review provides a comprehensive synthesis of mulberry’s taxonomy, distribution, nutritional and phytochemical profile, and its broad spectrum of health-promoting properties. Key bioactive constituents—including flavonoids, anthocyanins, alkaloids, and stilbenes—exhibit potent antioxidant, antidiabetic, neuroprotective, hepatoprotective, and anticancer activities. The paper also reviews modern extraction and separation techniques for isolating these compounds and evaluates mulberry's industrial potential in functional foods, pharmaceuticals, cosmetics, and biomaterials. Despite extensive preclinical evidence, challenges such as limited human clinical trials, lack of standardization, and regulatory hurdles remain. Future research should focus on clinical validation, bioavailability enhancement, and sustainable commercialization. Overall, mulberry represents a valuable natural resource with significant potential for public health, nutraceutical innovation, and sustainable industry.

**Keywords:** Medicine; *Morus* sp.; nutritional composition; phytochemicals; sericulture

**1. Introduction:**

Chronic health conditions are long-term, slowly progressing diseases that are non-communicable [1], often leading to irreversible damage and economic burden. Physical inactivity [2] and poor diet [3] are key contributors to their rising prevalence. Various dietary patterns are linked to improved health outcomes [4]. Mulberry being a rich source of different macro and micro nutrients (Fig 1) are used in prevention of cardiovascular diseases, diabetes, and certain cancers [5].

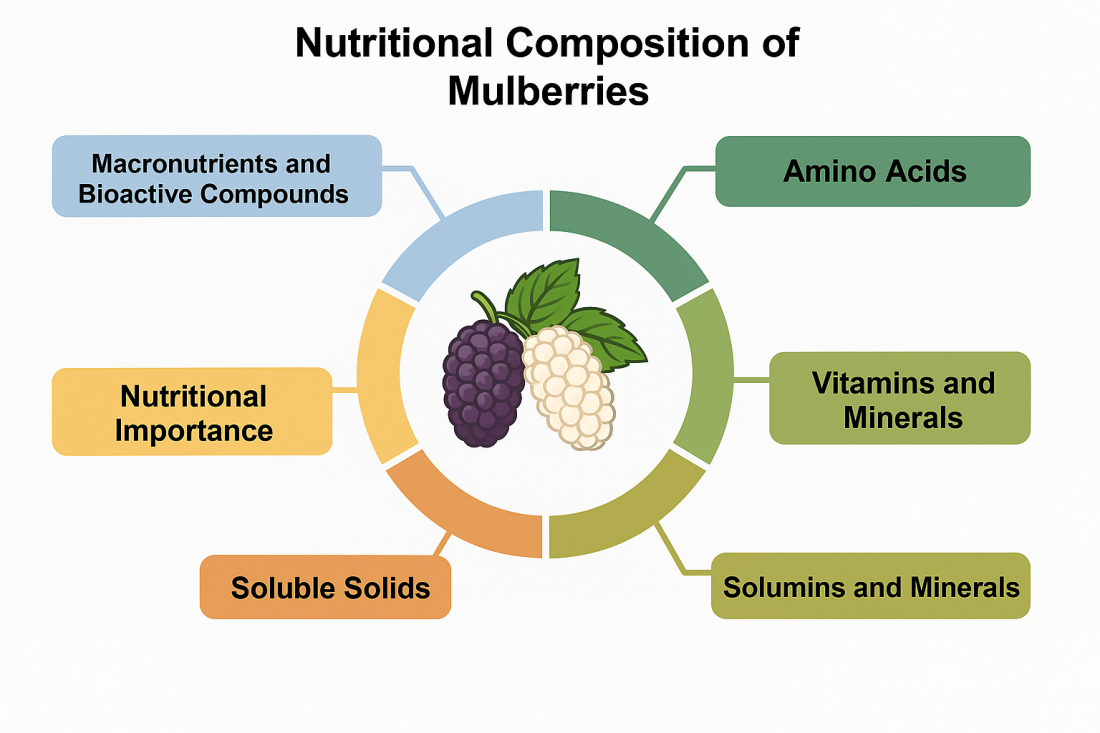


Fig1: Different nutritional components of mulberry

Historically, mulberry has been valued since the Tang Dynasty (AD 659) and is featured in classic medical texts. The 2020 Chinese Pharmacopoeia recognizes Morus alba L. for nourishing Yin and blood, and moistening dryness. Globally, mulberry is consumed as both food and medicine due to its rich content of vitamins (A, B, C, K, E), fatty acids, organic acids, minerals (Mg, Fe, K, Ca), proteins, amino acids, sugars, and fiber [6,7,8]. It also exhibits antioxidant, hypoglycemic [9], anticancer [10], antibacterial, and lipid-lowering properties [11].

However, comprehensive evaluations of its nutrient structures, properties, mechanisms of action, and bioavailability are lacking. Clinical applications remain underexplored. This review aims to summarize the nutritional value, health benefits, and applications of mulberry in food, biomaterials, and medicine, to support drug development, functional foods, and public health strategies.

**2. Taxonomy, distribution, and varietal diversity**

Mulberry, belonging to the genus Morus, is one of the most medicinally significant plants. India hosts over 20 mulberry species, with M. latifolia, M. indica, M. serrata, and M. alba being the most commonly cultivated varieties [12]. These fast-growing, perennial, and deep-rooted plants can be either monoecious or dioecious, reaching heights of 10–12 meters. Mulberries are widely distributed across regions including India, China, Japan, North Africa, Arabia, and Southern Europe. The Morus genus includes around a dozen species, adaptable to both tropical and temperate climates. They thrive under rainfed or irrigated conditions, with optimal growth at temperatures between 24–29°C and humidity levels of 65–80%. While two species are native to the United States, others are spread throughout the warmer temperate zones of Eurasia, Africa, and North America. Characterized by their milky sap, these plants produce fruits that have given them their name.

Morus alba (white mulberry), the primary food for silkworms, is extensively cultivated in its native China. Unlike the red or black berries typical of most Morus species, the fruit of white mulberry ranges from white to pinkish and is also found in the Eastern United States. Historically, M. alba has been used in traditional Chinese medicine since A.D. 659. The Chinese Pharmacopoeia (1985) lists various parts of the plant—including leaves, root bark, branches, and fruits—as components of medicinal formulations, while other parts like the sap and wood ash are also commonly utilized.

**3. Nutritional composition of mulberry:**

Mulberries are packed with essential functional components that play vital roles in promoting human health. Structurally, the fruit comprises approximately 71.4% pulp, 23.5% skin, 2.9% seeds, and 2.2% stems. Their high moisture content makes them difficult to preserve, yet they remain nutritionally rich, offering a variety of macro- and microcompounds:

• **Macronutrients and Bioactive Compounds**: Mulberries contain 0.5–1.4% protein and approximately 7.8–9% carbohydrates [13]. They also include 0.3% to 0.5% fatty acids, 1.1% to 1.8% free acids, and 0.9% to 1.3% crude fiber. The primary fatty acids—linoleic, oleic, palmitic, and stearic acids—make up 69.66–78.02% of total fatty acids [14].

• **Amino Acids**: Nineteen amino acids have been detected in mulberries, with seven being essential for humans. Glutamate is the most prevalent (~20%), followed by glycine and aspartate [15]. Other amino acids include lysine, leucine, isoleucine, histidine, threonine, tryptophan, and serine. Notably, leucine, threonine, isoleucine, glycine, valine, tryptophan, arginine, aspartic acid, and serine are found in greater amounts in white mulberry, while black mulberry contains higher levels of lysine, histidine, and proline [16].

• **Carbohydrates and Organic Acids**: Mulberries are rich in neutral sugars such as arabinose, galactose, glucose, rhamnose, xylose, and mannose, alongside significant quantities of uronic acids like galacturonic acid and glucuronic acid [17–20]. They also contain organic acids including succinic, acetic, malic, citric, and tartaric acids [21]. The titratable acid content ranges from 0.20–2.65%, with black mulberry exhibiting higher concentrations [16, 22].

• **Vitamins and Minerals**: Key vitamins in mulberries include vitamin C, vitamin A, and several B-complex vitamins [23]. They are also abundant in minerals such as calcium (Ca), potassium (K), sodium (Na), phosphorus (P), iron (Fe), magnesium (Mg), zinc (Zn), copper (Cu), nickel (Ni), and selenium (Se). Notably, mulberries contain 5 to 20 times more selenium than apples, offering significant benefits for cardiovascular health and immune function [24].

• **Soluble Solids**: Sugars, acids, vitamins, and minerals contribute to the fruit’s flavor and nutritional value. The total soluble solid content varies between 6.2% and 25.8% [22, 16, 25, 26].

• **Nutritional Importance**: These nutrients collectively support vital physiological and metabolic functions, bolster immune defenses, and aid in glucose regulation [13, 27, 28].

**4. Phytochemicals and Bioactive Compounds**

Mulberry serves as a rich reservoir of diverse phytochemicals and bioactive constituents that significantly enhance its nutritional and therapeutic importance. These are seen depicted in figure 2. The most extensively researched compounds include polyphenols, flavonoids, anthocyanins, alkaloids, polysaccharides, stilbenes, and benzofurans. These bioactives are associated with a wide range of health-promoting effects, such as antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, and neuroprotective activities. The levels and types of these compounds can vary greatly depending on several variables, notably the Morus species, the specific plant part used, the stage of maturity, and environmental influences. For instance, Morus nigra (black mulberry) typically exhibits higher concentrations of total phenolics, flavonoids, and anthocyanins when compared to M. rubra and M. alba [22, 24, 29].

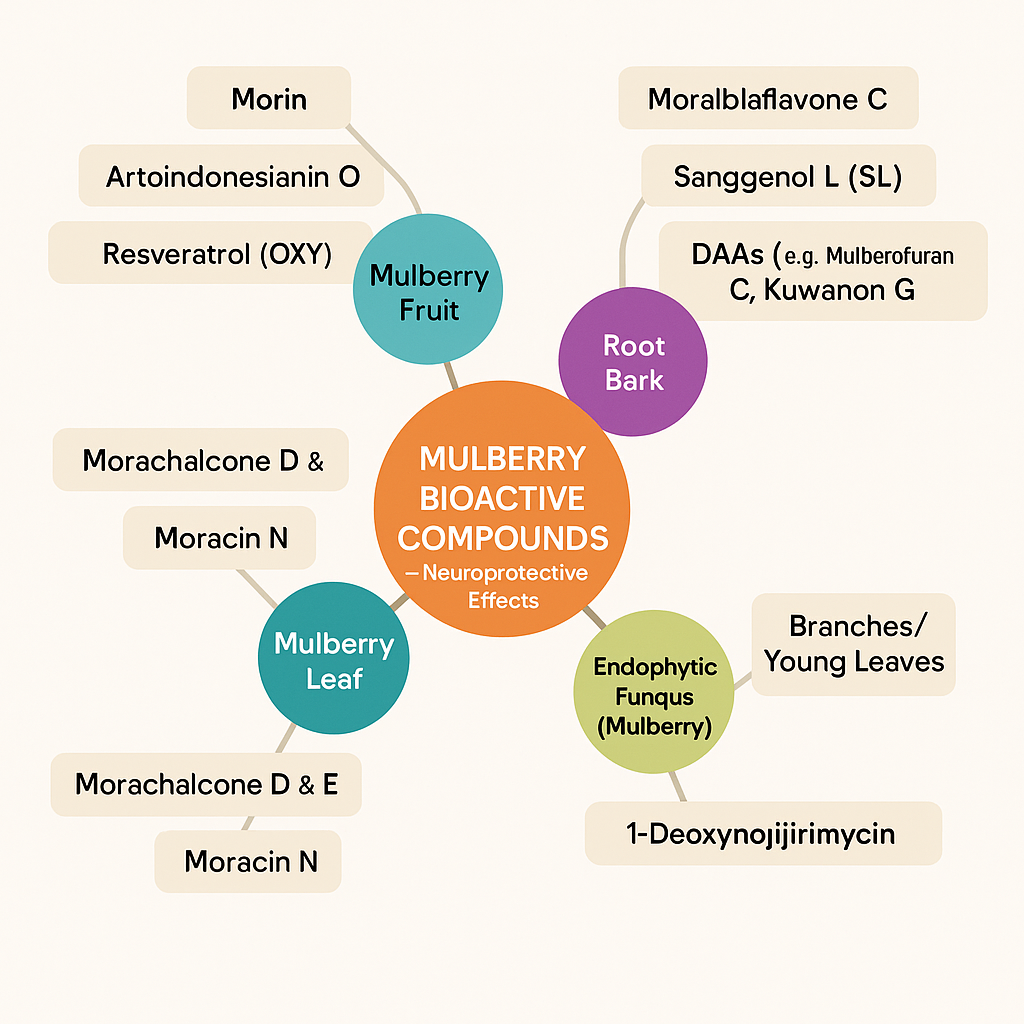


Fig 2: Phytochemicals and bioactive constituents in mulberry

Beyond species differences, environmental and geographical conditions significantly affect the phytochemical profile. Factors such as climate, soil composition, agricultural practices, and elevation can all impact the accumulation of bioactives in mulberry fruits [23, 30, 31]. Comparative studies of mulberries from various regions have shown marked differences in total phenolic content, ranging from 181–1422 mg GAE/100g FW in samples from Turkey to 547.60 mg GAE/g MAE in those from Hangzhou, China [22, 32]. Similarly, total flavonoid concentrations ranged from 29–276 mg QE/100g FW in Turkish varieties [22] to as much as 893.73 mg RE/g in anthocyanin extracts from Chinese mulberries [32]. These variations highlight the importance of region-specific assessment and standardization of mulberry cultivars to maximize their health-related properties. Recognizing and understanding these species- and location-specific differences in phytochemical content is vital for the effective development of mulberry-based nutraceutical and functional food products.

**4.1. Flavonoids**

Flavonoids are natural polyphenolic compounds with notable neuroprotective effects. In mulberry, they are grouped into flavonols, dihydroflavones, anthocyanins, and chalcones.

**4.1.1. Flavonols**

Flavonols (3-hydroxyflavones) display antioxidant, antibacterial, hepatoprotective, and anti-inflammatory properties [33].

* *Morin* reduces oxidative stress and improves cognition in sleep-deprived mice (5–20 mg/kg•b.w.) [34]; it also inhibits astrocyte activation and NF-κB in PD models [35], and promotes mitophagy via AMPK-ULK1/TFEB signaling [36].
* *Moralbaflavone C* (10 μmol/L) protects PC12 cells from oxidative stress, surpassing edaravone [37].
* *Sanggenol L* restores PI3K/Akt/mTOR signaling and promotes autophagy in rotenone-damaged SK-N-SH cells [38].

**4.1.2. Anthocyanins**

*Cyanidin-3-glucoside (C3G)* is the main anthocyanin in mulberry, known for antioxidant and anti-inflammatory effects [39, 40].

* C3G protects against brain ischemia in MCAO mice [41], improves PC12 cell viability (10–30 μg/mL) [41], and maintains mitochondrial membrane potential in OGD-injured neurons [42].

**4.1.3. Chalcones**

Chalcones exhibit neuroprotective and antioxidant effects by inhibiting NF-κB [43–45].

* *Morachalcone D and E* protect HT22 cells from oxidative stress and ferroptosis. Morachalcone D (20–40 µmol/L) activates Nrf2 and upregulates GPx4, CAT, and SOD [46].

**4.2. Diels-Alder-Type Adducts (DAAs)**

Formed via [4+2] cycloaddition, DAAs in mulberry include potent neuroprotectives like *mulberrofuran C, J, G, K,* and *kuwanon G* [47, 48].

* Mulberrofuran C is ~3× stronger than Trolox and inhibits Aβ42 aggregation (56–70%) [49].
* Kuwanon G inhibits tau aggregation (96%) [49]; several DAAs also inhibit AChE, BuChE, and BACE1 (IC₅₀ = 1.4–2.7 µmol/L) [49].
* *Mulberrofuran K* crosses the blood–brain barrier and protects HT22 cells from glutamate toxicity [49].

**4.3. Benzofurans**

* *Artoindonesianin O* reverses tau hyperphosphorylation and Aβ42/NMDA-induced damage, improving synaptic plasticity [50].
* *Moracin N* reduces ROS and Fe²⁺ in HT22 cells and restores antioxidant defense (EC₅₀ = 0.4 µmol/L) [51].

**4.4. Quinones**

* *Evariquinone*, from *Colletotrichum* sp., inhibits ROS and Ca²⁺ overload in HT22 cells, downregulating MAPK pathways and preventing apoptosis [52].

**4.5. Stilbenes**

* *Mulberroside A* protects neurons from OGD/R-induced damage by suppressing ERK/JNK/p38 signaling [53] and improves gut-brain integrity in HFrD models [54].
* *Resveratrol* enhances mitochondrial biogenesis and reduces apoptosis in epilepsy models via PGC-1α, NRF1, and COX1 [55].
* *Oxyresveratrol* protects SH-SY5Y cells from 6-OHDA neurotoxicity but shows condition-specific effects [56, 57].

**4.6. Alkaloids**

* *1-Deoxynojirimycin (DNJ)*, abundant in branches, improves learning, reduces Aβ and inflammation, and downregulates BACE-1 in SAMP8 mice [58]. In insulin-resistant cells, DNJ (5 µmol/L) restores PI3K/AKT signaling, lowers tau phosphorylation, and boosts IDE expression [59, 60].

**5. Extraction and Separation Methods:**

Modern techniques have significantly advanced the extraction and analysis of bioactive compounds from mulberry (Morus spp.), offering improved efficiency and precision. While traditional methods like solid-liquid extraction (SLE) remain common, innovative approaches such as microwave-assisted extraction (MAE), ultrasonic-assisted extraction (UAE), supercritical fluid extraction (SFE), pressurized liquid extraction (PLE), enzymatic-assisted extraction (EAE), and solid-phase extraction (SPE) have enhanced yields and preserved compound stability. For example, MAE uses electromagnetic waves to rapidly heat solvents and tissues, while UAE relies on cavitation to disrupt plant cells and release phenolics and flavonoids.

SFE, particularly with supercritical CO₂, is favored for its environmental benefits and effectiveness, outperforming Soxhlet extraction by 1.15 times for non-polar compounds in M. alba and M. nigra leaves [61]. Successful extractions include α-amyrin acetate from M. alba root bark (3.68 ± 0.32 mg/g at 60°C, 20 MPa) [62] and β-sitosterol from leaves (30 MPa) and stem bark (40 MPa) [63]. However, high equipment costs limit SFE's wider use.

SPE is widely used for both extraction and purification. It enhanced anthocyanin analysis from M. nigra using HPLC [64] and helped identify aroma-active compounds such as benzaldehyde and (E)-2-nonenal in various mulberry species [65]. To overcome co-extraction of unwanted substances, combined techniques like SLE with enzymatic treatment or MAE with SPE are often employed. Ultrasound-assisted enzymatic extraction of M. nigra resulted in higher yields of phenolics, flavonoids, and anthocyanins than individual methods [66].

For compound separation and identification, chromatography methods such as macroporous resin adsorption (MAR), silica gel chromatography (SGC), ion exchange chromatography (IEC), gel filtration chromatography (GFC), preparative liquid chromatography (PLC), and countercurrent chromatography (CCC) are utilized. MAR relies on non-covalent interactions, while IEC effectively isolates charged compounds like DNJ and polysaccharides using DEAE-cellulose. These are often paired with analytical tools like GC, HPLC, and MS for accurate characterization [19].

Despite their advantages, limitations persist. SFE struggles with polar compounds; PLE and MAE may cause thermal degradation; EAE is hindered by enzyme specificity; and SPE remains largely lab-scale. While MAR, SGC, IEC, and GFC are more suited to preliminary screening, PLC and CCC, though effective, are costly and less scalable [67]. combining advanced extraction with chromatographic separation has greatly improved mulberry phytochemical profiling. Yet, challenges in scalability, cost, and method-specific constraints must be addressed for industrial application and commercialization.

**6. Pharmacological activities and mechanisms of mulberry**

The following table 1 summarizes the key pharmacological activities of mulberry (Morus spp.) along with their associated bioactive compounds, underlying molecular mechanisms, and corresponding therapeutic effects. This comprehensive overview highlights how mulberry's diverse phytochemicals contribute to its wide-ranging health benefits, supporting its potential as a functional food and therapeutic agent.

**7. Applications in Traditional and Modern Medicine**

Mulberry (Morus spp.) has a rich history in traditional medicinal systems like Traditional Chinese Medicine (TCM) and Ayurveda, used to treat ailments such as fever, hypertension, liver disorders, and diabetes. In TCM, Morus alba (white mulberry) has been used since A.D. 659, with the Chinese Pharmacopoeia (1985) documenting the use of its leaves, root bark, branches, fruits, sap, and wood ash. The leaves possess diaphoretic and emollient properties, soothing throat irritation and supporting skin health. The root bark ("Sang bai pi") is notable for treating cough, asthma, high blood pressure, and shows anti-HIV activity. In Ayurveda and Unani, mulberry serves as a purgative, vermifuge, and anti-inflammatory agent. Its fruit juice is traditionally used for diarrhea, malaria, and throat infections due to its refrigerant and laxative effects [82].

In modern medicine, mulberry is commonly found as Syrupus Mori in the British Pharmacopoeia, used as a flavoring agent and sore throat gargle [83]. Ethnobotanical studies also report its use for urinary incontinence, tinnitus, constipation, depression, and menopausal symptoms. Mulberry fruit wine is consumed for detoxification and blood purification. Ayurvedic decoctions from mulberry fruits are used against chronic nephritis, nasopharyngeal cancer, and arteriosclerosis. In Unani medicine, Morus nigra (black mulberry), known as “Tut-i-aswad,” is valued for anti-cancer properties [84]. Herbal combinations with Radix Glycyrrhizae and Cortex Poriae are prescribed for edema, thick sputum cough, and fever [85].

Scientific research increasingly supports these uses by identifying active compounds like flavonoids (morusin, quercetin), anthocyanins, and alkaloids (deoxynojirimycin), reinforcing mulberry’s role in integrated medicine and phytopharmaceuticals [83].

**8. Neuroprotective Effects of Mulberry Compounds**

Mulberry exhibits strong neuroprotective properties due to bioactive phytochemicals such as flavonoids, anthocyanins, Diels–Alder adducts, benzofurans, quinones, and stilbenes. These target key mechanisms in neurodegenerative diseases like Alzheimer’s (AD) and Parkinson’s (PD), including oxidative stress, protein aggregation (Aβ and tau), mitochondrial dysfunction, and neuroinflammation.

**8.1.** **Antioxidant Defense Mechanism**

Oxidative stress from excessive reactive oxygen species (ROS) is central in AD and PD pathology [86]. Mulberry extracts and compounds such as morin, cyanidin-3-glucoside (C3G), and mulberroside A boost antioxidant enzymes (SOD, GPx, CAT), increase glutathione (GSH), and reduce oxidative markers like MDA [34, 41, 46, 53]. For example, morin protected mouse hippocampus by modulating antioxidants and enhancing mitophagy via the AMPK-ULK1-TFEB pathway [36]. C3G safeguarded rat cortical neurons from mitochondrial depolarization in oxygen-glucose deprivation models [42].

**8.2.** **Inhibition of Aβ Aggregation**

Aβ aggregation is a hallmark of Alzheimer’s. Diels–Alder adducts such as mulberrofuran C, kuwanon G, and albafuran C inhibited Aβ42 fibril formation by 56–70%, comparable to resveratrol and methylene blue. These also blocked tau aggregation, with kuwanon G achieving 96% inhibition, surpassing methylene blue’s 80% [49]. Mulberry leaf methanol extract shortened Aβ fibrils and preserved hippocampal neurons in toxicity assays [87].

**8.3. Anti-Inflammatory Pathways**

Mulberry phytochemicals reduce pro-inflammatory cytokines IL-1β, IL-6, and TNF-α [53]. Mulberroside A effectively modulated ERK1/2, JNK1/2, and p38 MAPK pathways, suppressing neuroinflammation in cortical neuron models [53]. In vivo, it restored blood-brain barrier integrity and reduced hippocampal inflammation from high-fructose diet neurotoxicity [54].

**8.4. Mitochondrial and Synaptic Protection**

Compounds like resveratrol and oxyresveratrol improved mitochondrial function, DNA expression, and reduced apoptosis in neurodegeneration models [55, 56]. Artoindonesianin O (AIO), a benzofuran derivative, inhibited tau hyperphosphorylation, restored ATP production, and promoted dendritic spine regeneration and synaptic plasticity [50].

**8.5. Ferroptosis Inhibition**

Ferroptosis, an iron-dependent cell death, is a new neurodegeneration target. Morachalcone D and moracin N suppressed ferroptosis by maintaining GSH, inhibiting Fe²⁺ accumulation, and upregulating antioxidant genes like GPx4 and Nrf2 pathways [46, 51].

**8.6. Blood–Brain Barrier (BBB) Permeability**

Some mulberry compounds, including kuwanon H and mulberrofuran K, showed promising BBB permeability in PAMPA assays, indicating CNS access for therapeutic action [49]. Mulberrofuran K also protected HT22 cells from glutamate toxicity by increasing GSH and reducing ROS.

### ****9. Industrial applications and commercialization potential of mulberry****

Mulberry (Morus spp.) exhibits broad industrial potential due to its rich phytochemicals and traditional medicinal use. As demand for natural and health-promoting products grows, mulberry-based derivatives are increasingly commercialized across functional foods, pharmaceuticals, cosmetics, and biomaterials.

**9.1. Functional Foods and Beverages**

Mulberries, rich in polyphenols, flavonoids, anthocyanins, and vitamins, are used to create various health-oriented products. These include mulberry syrup, which retains stable phenolics and anthocyanins for 30 days and offers antioxidant benefits [88]; mulberry wine, known for strong free radical scavenging [89]; mulberry vinegar, which modulates neuroinflammation via NF-κB and glial pathways [80]; and mulberry enzyme that improves gastrointestinal motility and relieves constipation [90]. Additionally, mulberry yogurt boosts antioxidant activity and gut health, while mulberry jelly, enhanced with inulin, supports probiotic growth and sensory quality [91]. These uses highlight mulberry’s versatility in nutraceuticals and functional food development.

**9.2. Natural Colorants and Additives**

Mulberry anthocyanins are promising natural food colorants, providing vibrant pigments and antioxidant effects. They offer a safer alternative to synthetic dyes, improving both nutrition and appearance in foods [92]. This also opens industrial-scale production opportunities, especially in mulberry-cultivating tropical sericulture regions.

**9.3. Cosmetic and Dermatological Applications**

Compounds like resveratrol and flavonoids reduce oxidative stress, promote hyaluronic acid and collagen synthesis, and inhibit melanin production, leading to anti-aging creams, sunscreens, and whitening products [88].

**9.4. Pharmaceutical Uses**

Beyond traditional systems like Ayurveda and TCM, mulberries contribute to modern pharmaceuticals. Syrupus mori from ripe fruits is used for sore throat and cough, leveraging antioxidant and immune-supportive effects. Flavonoids and alkaloids such as morusin, mulberrofuran D, and 1-deoxynojirimycin exhibit antiviral, antidiabetic, and anticancer properties, highlighting pharmaceutical potential [83, 88].

**9.5. Biomaterials and Packaging Innovations**

Mulberry compounds are applied in biomaterials like films, wound dressings, and smart food packaging. For example, polyvinyl alcohol/tapioca starch films with mulberry anthocyanins and lauroyl arginate serve as natural spoilage indicators and extend shelf life [93]. In biomedical uses, mulberry polyphenols enhance wound dressings through antimicrobial and anti-inflammatory effects, promoting healing and infection control.

**9.6. Emerging Products and Future Prospects**

Mulberry’s potential is expanding with products like mulberry milk, which inhibits cortisol and improves memory [94]; mulberry fruit powder for yogurt fortification [95]; and energy bars and dietary supplements. Its bioactives function as food preservatives, colorants, and therapeutic agents, supporting sustainable product innovation. However, future industrial success depends on advances in bioavailability, standardization, and regulatory approval [88].

### ****10. Challenges and future prospects****

### Despite the extensive pharmacological and industrial potential of mulberry (Morus spp.) and its derivatives, several challenges remain that must be addressed to support its widespread adoption and commercialization.

**10.1. Lack of Standardized Methodologies and Global Acceptance**

One of the major limitations hindering the broader use of mulberry in food, pharmaceutical, and cosmetic industries is the **lack of standardized extraction, purification, and quantification protocols**. Differences in extraction solvents, plant parts used, harvest timing, and analytical methods lead to inconsistent results across studies, making it difficult to compare findings or develop universally accepted formulations. Furthermore, the absence of globally recognized **quality control parameters**, particularly for bioactive-rich extracts like anthocyanins, flavonoids, or DNJ, impedes their inclusion in regulatory frameworks and official pharmacopeias. Establishing **Good Agricultural and Collection Practices (GACP)** and **Good Manufacturing Practices (GMP)** tailored to mulberry could help bridge this gap and increase international credibility and acceptance.

**10.2. Need for Clinical Trials and Regulatory Approval**

Although numerous **in vitro and in vivo studies** have demonstrated the therapeutic efficacy of mulberry bioactives—including antidiabetic, neuroprotective, anticancer, and antioxidant effects—**clinical evidence in humans remains limited**. The majority of existing studies focus on cell lines or animal models, with few progressing to human trials. Without robust **randomized controlled trials (RCTs)**, it is challenging to verify dosage, safety, efficacy, or potential side effects in human populations. Additionally, regulatory approval from agencies like the FDA, EFSA, or WHO requires comprehensive toxicological, pharmacokinetic, and long-term safety data. This regulatory uncertainty poses a significant barrier to the full-scale commercial application of mulberry-based nutraceuticals and therapeutic agents.

**10.3. Future Research Directions**

To unlock the full potential of mulberry, future research should adopt **integrated, high-throughput, and precision-based approaches**.

* **Omics technologies**—including genomics, transcriptomics, proteomics, and metabolomics—can elucidate the biosynthetic pathways of bioactives like anthocyanins, stilbenes, and alkaloids, and identify key regulatory genes for metabolic engineering or breeding programs.
* **Pharmacokinetic studies** are essential to determine the absorption, distribution, metabolism, and excretion (ADME) of individual mulberry phytochemicals, particularly in complex human systems. Understanding bioavailability and half-life will support optimized dosing and delivery.
* **Nanotechnology-based delivery systems**, such as nanoemulsions, liposomes, and polymeric nanoparticles, represent a promising strategy to improve the stability, solubility, and targeted delivery of mulberry bioactives. These systems could help overcome limitations associated with poor water solubility, rapid metabolism, or degradation in the gastrointestinal tract.

**11. Conclusion:**

Mulberry (Morus spp.) stands as a multifunctional plant with deep roots in traditional medicine and expanding relevance in modern science. Rich in nutrients and bioactive compounds, it exhibits wide-ranging therapeutic properties that support its integration into functional foods, phytopharmaceuticals, and natural health products. Advances in extraction technology and phytochemical analysis have paved the way for innovative applications in cosmetics, food preservation, and biomaterials. However, critical challenges persist, particularly the need for standardized processing methods, human clinical evidence, and regulatory approval. Interdisciplinary research leveraging genomics, pharmacokinetics, and nanotechnology holds promise for unlocking mulberry’s full medicinal and industrial potential. As interest in natural and sustainable health solutions grows, mulberry emerges as a compelling candidate for future innovations in health and industry.

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**Table 1:** Pharmacological Activities, Bioactive Compounds, Mechanisms, and Therapeutic Effects of Mulberry (Morus spp.)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Activity** | **Major Bioactive Compounds** | **Mechanism of Action** | **Therapeutic Effect** | **References** |
| **Antioxidant** | Polyphenols, Flavonoids, Anthocyanins, Polysaccharides, C3G, Resveratrol | Scavenging ROS, upregulating GSH and SOD, redox homeostasis | Protection from oxidative stress and cellular damage | [68, 69] |
| **Anti-inflammatory** | Quercetin, Rutin, Anthocyanins | Downregulation of TNF-α, IL-6, NO; inhibition of NF-κB, MAPK pathways | Suppression of chronic inflammation | [19, 70, 71] |
| **Anticancer** | Polyphenols, Polysaccharides | Activation of caspases, p53 upregulation, modulation of Bax/Bcl-2 | Induction of apoptosis and cell cycle arrest in cancer cells | [72, 73] |
| **Antidiabetic** | 1-Deoxynojirimycin (DNJ), Flavonoids, Polysaccharides | Inhibition of α-glucosidase, improved insulin sensitivity, β-cell protection | Glycemic control, adjunct to diabetes management | [74, 75] |
| **Hepatoprotective** | MFPs, MLPs | Reduction of liver enzymes, inhibition of lipid peroxidation, enhancement of antioxidants | Protection against liver injury | [70, 76] |
| **Hypolipidemic** | Flavonoids, Polysaccharides | Modulation of lipid metabolism, increased HDL, decreased LDL and triglycerides | Management of dyslipidemia and prevention of cardiovascular disease | [74, 77] |
| **Neuroprotective** | Morin, C3G, Chalcones | Antioxidant, anti-inflammatory, anti-apoptotic effects; regulation of AMPK, Nrf2 | Neurodegeneration prevention and cognitive enhancement | [36, 42] |
| **Antibacterial** | Flavonoids, Alkaloids, Phenolic acids | Disruption of bacterial membranes, enzyme inhibition | Inhibition of pathogens like *S. aureus* and *E. coli* | [78] |
| **Immunomodulatory** | Polysaccharides | Stimulation of macrophages, IL-2 and IFN-γ secretion | Enhanced immune function and resistance to infection | [79, 80] |
| **Mechanistic Summary** | - | Suppression of oxidative stress, NF-κB/COX-2 inhibition, autophagy and apoptosis regulation | Broad-spectrum therapeutic effects in chronic and degenerative diseases | [81] |