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# ENHANCING THE STABILITY AND BIOAVAILABILITY OF MULBERRY EXTRACTS IN FOOD PRODUCTS

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**ABSTRACT**

Mulberry (*Morus spp*.), including *M. alba, M. nigra* and *M. rubra*, is a healthful and medicinal fruit that has been used for a long time in traditional medicine. Even though cherries are rich in antioxidants, anthocyanins, flavonoids and phenolic compounds, their limited usage in industry is caused by how quickly they spoil and because all processing methods are not standardized. In this review, we study what mulberry fruit and leaves are made of, how they benefit health and how they are extracted, putting special emphasis on bioactive compounds. Many techniques, enzyme-assisted, ultrasound-assisted, microwave-assisted and high-speed shear homogenization, have been investigated to see if they can boost bioactive compound yield and keep them stable. Moreover, the work focuses on microencapsulation and functional foods, showing how it can lead to better antioxidant absorption, better digestion and advantages for diabetes, heart disease, brain health and cancer. The results highlight the need for new processing technologies to make mulberry a reliable and useful source of nutrients in the nutraceutical and food fields.

## 1. INTRODUCTION

Mulberry, which is in the genus Morus of the family Moraceae, is a deciduous tree that is broadly distributed in temperate to subtropical areas, with the following species being notable: *Morus alba* (white mulberry), *Morus nigra* (black mulberry), and *Morus rubra* (red mulberry) (Jan *et al.,* 2021). This is a versatile plant that has been grown for centuries, mainly for its leaves, which are used as the exclusive food source for silkworms, but its fruits, leaves, bark, and roots have been used in traditional medicine in a variety of medicine systems, such as Ayurveda, Unani, and Chinese medicine. The fruit, which is also popularly known as "shahtoot" or "toot" in a few cultures, is very perishable because it contains an extremely high percentage of water content (~88%) and is not easy to store fresh, although it is generally processed into jam, juice, wine, and other value-added forms to provide a longer shelf life and greater utility (Kattil *et al.,* 2024).

Mulberries (*Morus spp.)* consist of a wide variety of types, with different traits as far as fruit color, taste, and versatility. The three major species are *Morus alba* (white mulberry), whose sweet but generally weak-flavored fruits may be white, lavender, or black, and which has been used historically for silkworm culture. *Morus rubra* (red mulberry), a native of North America, valued for its black to reddish fruits with intense, balanced flavor and *Morus nigra* (black mulberry), which has large, juicy, strongly flavored dark purple berries, are usually regarded as being the best for cooking purposes. Hybrid varieties such as 'Illinois Everbearing' (*M. alba* × *M. rubra*) offer hardiness with superior fruit quality, while dwarf types such as 'Dwarf Everbearing' are well suited for limited space. Regional specialties such as 'Pakistan' (*M. macroura*) have exceptionally long, seedless berries, and ornamental varieties such as the contorted mulberry *(M. alba 'Unryu'*) provide distinctive beauty. The broad adaptability of mulberries, from temperate to subtropical environments, and their differing pollination requirements (some being self-fertile) also add to their horticultural diversity (Donno *et al.,* 2018). Mulberries contain several necessary nutrients such as carbohydrates (9.8% fresh weight), dietary fiber (1.7%), as well as limited amounts of protein and fat. They are especially known for having high amounts of vitamin C (51 mg per serving) and iron (2.6 mg per serving). Additionally, mulberries make a good source of potassium, vitamin K and vitamin E which benefit our heart, help metabolize bones and act as antioxidants accordingly (Martins *et al.,* 2023).

Mulberries are rich in important chemicals and their phytochemicals include different antioxidants including anthocyanins (cyanidin-3-glucoside, cyanidin-3-rutinoside), flavonols (quercetin and rutin), phenolic acids (chlorogenic acid) and alkaloids (DNJ or 1-deoxynojirimycin). This means that the antioxidant, anti-inflammatory and anti-hyperglycemic impact of a fruit is closely connected to the range of colours it can have, including white, light purple and deep purple. DNJ, a substance mainly found in mulberry leaf and fruit, acts by restraining the body's absorption of carbohydrates after meals. This could be used in addition to medication in diabetes treatment (Zhang *et al.,* 2018).

Mulberries may help improve the functions of the heart and blood vessels. It has been reported that consuming mulberries can reduce your total cholesterol, LDL cholesterol and triglyceride levels and raise HDL cholesterol, making them beneficial in avoiding atherosclerosis and its effects. This occurs because the fruit helps to process fats in the body while lowering oxidative stress, as indicated by the fruit's high antioxidants seen in assays like ORAC. Moreover, resveratrol and rutin in the polyphenols group help manage hypertension and promote healthier endothelial function. In studies done on animals, mulberries have demonstrated the ability to protect the liver, fight cancer and shield the nervous system (Khalifa *et al.,* 2018).

The evidence suggests that flavonoids and anthocyanins in mulberries eliminate harmful free radicals, limit the growth of cancer cells and lower the risk of DNA damage. It might be able to control inflammation in the liver and prevent NAFLD by managing lipid peroxidation and improving the activity of antioxidant enzymes. Additionally, mulberry polyphenols can help protect the brain, can cross into it through the blood-brain barrier and can lower oxidative stress in the brain to prevent various learning and memory problems. Mulberries may be beneficial to our health and wellness, but they are often overlooked on the commercial scale which is below that of most other berries. Perishability, limited seasons for availability and the lack of a standardized way to extract bioactive ingredients are some barriers that prevent functional foods and nutraceuticals from using many herbs (Naeem, 2020). Nevertheless, advances in food technology such as freeze-drying, encapsulation, and fermentation are uncovering new avenues for mulberries to be used in stable and bioavailable form. Also, ongoing inquiry into the synergistic action of mulberry compounds in the presence of other functional ingredients could further enhance their health benefits and uses.

### 1.1. Nutritional composition of mulberry:

Mulberry holds several compounds of value including anthocyanins, phenols, flavonoids, etc., that can be applied in the development of nutraceutical supplements (Wen *et al.,* 2019 ; Hao *et al.,* 2022). Several reports identify the protective benefits of the phenolics contained in mulberry species on health such as protection against free radicals, cholesterol lowering, anti-inflammatory and diabetic regulators. It has been documented that mulberries contain gallic acid, chlorogenic acid, caffeic acid rutin, catechin, sringic acid, p-coumaric acid, ferulic acid, o-coumaric acid, phloridzin, protocatechuic acid and quercetin (Skrovankova *et al.,* 2022).

Mulberry fruit gets its bright color and antioxidant properties through the anthocyanins, which are flavonoids. In addition to making fruits and vegetables red, purple, and blue, anthocyanins have benefits for health and are also thought to protect against cancer and inflammation (Rohela *et al.,* 2020). In addition, mulberry helps to prevent damage to the liver, strengthens joints, helps release urine, and lowers blood pressure. Three anthocyanins present in mulberry fruit are cyanidin-3-o-glucoside, cyanidin-3-o-rutinoside, and pelargonidin-3-glucoside (Kim and Lee, 2020). Since it contains flavonoids and phenolics, mulberry is thought to act as a laxative, lower blood sugar, expel parasites, provide pain relief, and induce vomiting (Negro *et al.,* 2019). Being aware of key components and contents of mulberry is beneficial for the exploration of food using mulberry (Jan *et al.,* 2021). As mulberry is highly perishable and spoils easily, efforts should be made to use its fruit in several types of industrial products for better preservation (Jan *et al.,* 2021; Mahesh *et al.,* 2017). So far, reviews about mulberry have not covered the nutritional benefits of its seeds. Less knowledge is available on both the conventional and modern methods used to gather mulberry fruits. Mulberry fruits are drupes, just like other types of berries. Once pollinated, the ovary base of every female flower in catkin inflorescence gets enlarged, turns into a fruit, and changes in chemistry, color, and texture while maturing. Mulberries look a lot like raspberries and blackberries, except that they have stem-like stalks on each fruit. Fully ripened berries of several types have skin that is white, pink, deep red, black, violet black, or purplish black.

### 1.2. Physico-chemical composition of different mulberry fruits

Morus nigra is celebrated for its tasty and very juicy black fruit (Meena *et al.,* 2022). White mulberry fruits are found to have the highest total soluble solids, pH, and moisture compared to the other 2 types. Acidity plays a key role in judging the quality of fresh fruits. Fruits having a pH value lower than 3.5 will most likely taste sour (Gozlekci *et al.,* 2015). As a result, white mulberry fruits have a stronger flavor and taste well in their natural state or used in making fruit products. Even so, black mulberries tend to be slightly sour (contain the least acid and sugar) and are best used as functional food or medicine instead of fresh eating (Aydın *et al.,* 2016; Skender and Becirspahic, 2019; Parida and Rayaguru, 2021). Mulberry is rich in sugars, with fructose and glucose making up all of the sugar it contains. Black mulberry typically has the widest and longest mulberry fruit, and red mulberry has the smallest (Aljane and Sdiri, 2016; Gecer *et al.,* 2016; Skender and Becirspahic, 2019). Both previous studies and experimental findings suggest that red mulberry fruits have greater weight on average, compared to black and white mulberry (Gozlekci *et al.,* 2015; Aydın *et al.,* 2016; Grygorieva *et al.,* 2016; Skender and Becirspahic, 2019). A number of reports by researchers have shown that colors in Morus plant species range from white and red to deep purple, while their moisture content in black mulberry is usually high (Ali *et al.,* 2016; Gozlekci *et al.,* 2015; Saensouk *et al.,* 2022). Since mulberry is sweet and sour in character, the amount of soluble solids in mulberry is crucial and is known to reach its highest amount in white mulberries and its lowest in red (Aljane and Sdiri, 2016; Aydın *et al.,* 2016; Erogul *et al.,* 2014; Parida and Rayaguru, 2021; Skender and Becirspahic, 2019).

It is known that mulberry contains glucose (26.3 %) and fructose (8.1567 %), with a greater presence of glucose and fructose found in black mulberry. Arabinose, galactose, xylose, and mannose are other sugars found in sugar cane at lower amounts (Aljane and Sdiri, 2016; Chen *et al.,* 2016; Gecer *et al.,* 2016; Parida and Rayaguru, 2021). A study by Aydın *et al.* in 2016 revealed that red mulberry had the highest acid content and white mulberry had the least. Protein accounts for 7.66–16.70 % in mulberry fruits. While some studies found the red mulberry to have higher protein (16.70 %), others mention the percentage as 9.0–15.6 % (Koca el al 2008 ; Koyuncu et al 2014; Salcedo et al 2015). Black mulberry, according to the authors, had up to 17.97 % palmitic acid and 7.26 % oleic acid, while white mulberry contained less palmitic acid (77.90%) and more oleic acid (78.02%). While vitamin C is present in all types of Morus, researchers have reported the highest amount in white and red mulberries (87.49 mg/100 g) (EI-baz *et al.,* 2017; Salcedo *et al.,* 2016; Skrovankova *et al.,* 2022). Mulberry contains high levels of potassium, calcium, phosphorus, sodium, and magnesium as well as some zinc, nitrogen, copper, manganese, iron, riboflavin, and niacin. Parida and Rayaguru (2021) say that mulberry fruit, and particularly red mulberry, contains 435 mg of phenolics in every 100 g. Table 1 displays data on various physico-chemical traits found in all three mulberry species that all display good nutrients with some variation in the amount of protein, sugars, vitamins, essential micronutrients, and natural antioxidants called phenolics. Mulberry seed contains good nutrition and is safe for eating. Some people use seeds to treat microbes, but there is no evidence as to its effectiveness (Shukla *et al.,* 2015). The leaves of mulberry plants are also rich in nutrients and helpful substances. Mulberry leaves are taken by patients with diabetes as an anti-hyperglycemic supplement (Banu, *et al.,* 2015). Table 1 reported that mulberry seeds contain valuable amounts of protein (18.039-21.58%), carbohydrates (43.17– 68.14%), and total ash (3.5 to 6.90%).

**Table 1: Nutritional composition of mulberry**

| Component | Value (Range) | Notes |
|---|---|---|
| Moisture | 76–88% | Fresh fruit |
| Protein | 0.8–1.4% | |
| Fat | 0.1–0.4% | Low-fat content |
| Carbohydrates | 7.6–9.8% | Includes sugars |
| Dietary Fiber | 1.4–1.7% | |
| Ash | 0.5–0.7% | Represents total minerals |
| Vitamin C | 20–35 mg/100 g | High antioxidant content |
| Vitamin A | 0.01–0.07 mg/100 g | As β-carotene |
| Calcium | 36–39 mg/100 g | Essential for bone health |
| Iron | 1.8–2.6 mg/100 g | Beneficial for hemoglobin |
| Phosphorus | 38–57 mg/100 g | Supports energy metabolism |
| Potassium | 194–200 mg/100 g | Important for heart function |
| Anthocyanins | High (no specific value) | Pigments with antioxidant activity |
| Phenolic Compounds | Rich in gallic acid, rutin, etc. | Bioactive compounds |

According to Argon *et al.* (2019), Rahman *et al.* (2014), and Shukla *et al.* (2015), white mulberry contains 21.58% protein and 6.05 % ash, whereas the content of carbohydrates in black mulberry is reported to be 68.145% (A.D Sharma *et al.,* 2013). Besides providing protein (20.94–37.36%), abundance in minerals (14.78 %), and fibers (3.6–16.61 g/100 g), leaves from different species also contain carbohydrates (3.1–3.7 %). White mulberry contains the highest protein (37.36 %), fiber (16.61 g/100 g), and minerals (14.78 %) but black mulberry has the largest carbohydrates (3.7 %) (Dimitrova, 2015; Koyuncu *et al.,* 2014; Margareta *et al.,* 2015; Salcedo *et al.,* 2017; Yu *et al.,* 2018). Besides its moisture content, leaves also include a range of other substances like nitrogen, copper, iron, manganese, and so on. Journalists have reported that DNA methylation changes can be used to breed mulberries for various conditions in the future. Likewise, studies from literature present slight variations in the major nutrients found in black and white mulberry leaves and seeds.

The mulberry plant is rich in bioactive materials such as anthocyanins, phenols, flavonoids, and others, which can be used in making nutraceuticals (Wen *et al.,* 2019). Various studies have found phenolics in different mulberry species such as Morus alba, Morus nigra, Morus multicalis, Morus laevigata, Morus atropurpurea, and Morus rubra to help treat oxidative stress, lower blood sugar, decrease inflammation, and reduce cholesterol (Turan *et al.,* 2017). The foliage fruit contains many anthocyanins, which provide the natural color as well as antioxidants to the fruit. Besides making food look good, anthocyanins have several known health benefits, such as fighting inflammation, contributing to better health, and aiding in fighting cancer and improving chronic diseases (Rohela *et al.,* 2020). In mulberry, the main phenolic compounds found are gallic acid, chlorogenic acid, caffeic acid, and rutin. The amount of these found in black mulberry ranges from 0.164 - 38.5 mg/100 g, 1.778-90.8 mg/100 g, 0.094- 14.84 mg/100 g, and 0.82- 97.2 mg/100 g, respectively. Authorities report that white mulberry has 0.165-0.215 mg/100 g, 0.103–2.667 mg/100 g, 0.094–0.134 mg/100 g, and 0.128–3.882 mg/100 g of the different compounds, while red mulberry has 0.097–0.156 mg/100 g, 0.0101–3.778 mg Looking at these studies, it is found that black mulberries had a higher level of phenolic compounds than white and red mulberries. Besides the main three, mulberry fruits may have catechin, sringic acid, p-coumaric acid, ferulic acid, o-coumaric acid, phloridzin, protocatechuic acid, and quercetin in them as well (Eyduran *et al.,* 2015; Gundogdu *et al.,* 2011; Skrovankova *et al.,* 2022). Among anthocyanins in mulberry fruit, cyanidin-3-o-glucoside (c3g) had a concentration of 116.15–959.56 mg/g of dry matter, followed by cyanidin-3-o-rutinoside's (c3r) concentration of 572.1 mg/g in black mulberry. Other minor amounts of anthocyanins can be found in this food, such as pelargonidin-3-O-rutinoside (Kamiloglu *et al.,* 2013; Kim and Lee, 2020; Skender and Becirspahic, 2019).

**Table 2: Extraction of mulberry by different techniques**

| Source of Mulberry | Extracted Compound | Technique | Result / Activity | Reference |
|---|---|---|---|---|
| *Morus alba* leaf | Polysaccharides | Solid-liquid extraction | Antioxidant activity; $Fe^{2+}$ chelation; radical scavenging | Zhang *et al.* (2014a), Liao *et al.* (2017) |
| *Morus alba* fruit | Polysaccharides | Response surface method optimization | Optimal antioxidant activity | Deng, Zhou, and Chen (2014) |
| *Morus alba* leaf | Polysaccharides | Enzymatic/solvent extraction | Anti-diabetic, regulates glucose metabolism | Ren *et al.* (2015) |
| *Morus alba* fruit | Polysaccharides | Not specified | Modulates gut microbiota, enhances insulin signaling | Jiao *et al.* (2017) |
| *Morus alba* wood | Oxyresveratrol | Solvent extraction, chromatography | Neuroprotective, antioxidant, anti-inflammatory | Andrabi *et al.* (2004), Weber *et al.* (2012) |
| *Morus alba* twig | Anthocyanins (C3G, C3R) | Solvent extraction | Anti-cancer (inhibits A549 migration), antioxidant | Chen *et al.* (2006) |
| *Morus alba* root | Mulberroside A | Solvent extraction | Anti-hyperlipidemic, anti-inflammatory, neuroprotective | Jo *et al.* (2014), Wang *et al.* (2014) |
| *Morus alba* root | Moracins | Solvent extraction | Anti-Alzheimer's, antioxidant, anti-inflammatory | Seong *et al.* (2018), Lee *et al.* (2016) |
| Morus nigra stem | Kuwanons (C, G) | Solvent extraction | Antioxidant, antimicrobial, anti-inflammatory, neurogenic | Abbas *et al.* (2014), Kong *et al.* (2015) |
| *Morus alba* | Sanggenons (C, | Solvent extraction | Antioxidant, | Chen *et al.* |

| | | | | |
|---|---|---|---|---|
| twig | G, V) | | antimicrobial, anti-cancer (colon, influenza), anti-inflammatory | (2018), Grienke *et al.* (2016) |
| *Morus alba* leaf | DNJ (alkaloid) | Solid-liquid extraction | α-glucosidase inhibitor, anti-diabetic, neuroprotective | Kwon *et al.* (2011), Chen *et al.* (2018) |
| Morus bombycis | Fagomine | Solvent extraction | Anti-hyperglycemic, potentiates insulin secretion | Nojima *et al.* (1998), Taniguchi *et al.* (1998) |

In their study, Li *et al.* (2021) assessed the effects of extraction methods, in combination with superfine grinding pretreatment, on polysaccharides extracted from mulberry fruit (*Morus alba* L.); the structural, rheological, and antioxidant properties were analyzed. The mulberry fruit was subjected to superfine grinding and sieved through a 100-mesh sieve to reduce particle size and improve extraction efficiency. It was reasoned that the superfine grinding would break cellular bound structures, resulting in more intracellular polysaccharides being released. The hot-water extraction (HWE) method was used as the first extraction method, and a series of four different extraction methods were used: enzyme-assisted hot-water extraction (EAHE); ultrasonic-assisted hot-water extraction (UAHE); and high-speed shear homogenization-assisted hot-water extraction (HSEHE). All extraction methods used the same superfine ground powder with respective names as, MFP-HWE100, MFP-EAHE100, MFP-UAHE100, and MFP-HSEHE100. Extraction yields were consistent when comparing extraction methods, where the highest yield as noted with HSEHE, indicating that the mechanical forces during high-speed shear homogenization helped break down the plant matrix, releasing greater amounts of polysaccharides. In the case of HWE, there was a lower extraction yield, indicating that mechanical force was significant for the extraction yield efficiency.

**Table 3: Different extraction methods on mulberry and its impact on rheological properties and antioxidant properties**

| Extraction Method | Sample Code | Extraction Yield | Molecular Weight | Particle Size | Rheological Properties | Antioxidant Activities |
|---|---|---|---|---|---|---|
| Hot-Water Extraction (HWE) | MFP-HWE100 | Moderate | Higher | Larger | Lower thixotropy | Lower |
| Enzyme-Assisted Hot-Water Extraction (EAHE) | MFP-EAHE100 | Moderate | Moderate | Moderate | Moderate thixotropy | Moderate |
| Ultrasonic-Assisted Hot-Water | MFP-UAHE100 | Moderate | Moderate | Moderate | Moderate thixotropy | Moderate |

| | | | | | | |
|---|---|---|---|---|---|---|
| Extraction (UAHE) | | | | | | |
| High-Speed Shear Homogenization -Assisted Hot-Water Extraction (HSEHE) | MFP-HSEHE100 | Highest | Lowest | Smallest | Highest thixotropy | Highest |

Another study was conducted by Wang and Huang, (2024) different extraction techniques were applied on mulberry. Here is the detail of it in the following table

**Table 4: Different extraction techniques and their advantages and disadvantages on mulberry.**

| Extraction Method | Plant Part | Extraction Conditions | Advantages | Disadvantages |
|---|---|---|---|---|
| Hot Water Extraction (HWE) | Leaves, Fruits, Branches | 80–100°C, 1–3 hours | Simple, cost-effective | Lower yield, potential degradation of heat-sensitive compounds |
| Enzyme-Assisted Extraction (EAE) | Leaves, Fruits | Specific enzymes (e.g., cellulase, pectinase), 40–60°C | Higher yield, preserves bioactivity | Enzyme cost, requires precise control |
| Ultrasonic-Assisted Extraction (UAE) | Leaves, Fruits | Ultrasonic power 100–500 W, 30–60 minutes | Shorter extraction time, improved yield | Equipment cost, potential degradation if not controlled |
| Microwave-Assisted Extraction (MAE) | Leaves, Fruits | Microwave power 300–700 W, 5–20 minutes | Rapid extraction, high efficiency | Uneven heating, possible degradation |
| Alkali Extraction | Branches | NaOH solution, room temperature to 60°C | Effective for cell wall polysaccharides | Harsh conditions may alter polysaccharide structure |
| Acid Extraction | Branches | Dilute HCl or other acids, 60–90°C | Efficient for certain polysaccharides | Risk of hydrolysis, requires neutralization |

A study conducted by researchers from Hebei Agricultural University in 2025 evaluated 21 mulberry varieties for fruit quality using Principal Component Analysis (PCA), Entropy Weight Method (EWM), and Grey Relational Analysis (GRA). The study measured appearance quality (fruit diameter, shape index, color), nutritional quality (free amino acids, soluble proteins), functional components (polyphenols, anthocyanins), and antioxidant capacity. Results showed that varieties like 'Ri Ben Guo Sang' and 'Hong Guo 1' excelled in appearance, while 'Jiang Mi Guo Sang' and 'Da Yi Bai' ranked high in nutritional quality and antioxidant activity. The PCA identified seven principal components explaining 88.4% of variance, with 'Da 10' and 'He Lan Sang' emerging as top cultivars for comprehensive quality.

A study by Arfan *et al.* (2012) compared the antioxidant properties of *Morus nigra* and *Morus alba* fruits. Researchers extracted phenolic compounds using methanol and acetone, followed by sugar-free extraction (SFE) via Amberlite XAD-16 chromatography. Antioxidant capacity was assessed using ABTS, DPPH, and reducing power assays. *Morus nigra* exhibited higher total phenolics (164–173 mg/g) and stronger antioxidant activity (EC50: 48–58 µg/mL) than *M. alba* (EC50: 66–79 µg/mL). HPLC confirmed chlorogenic acid and rutin as dominant phenolics, with *M. nigra* containing higher concentrations. The study concluded that *M. nigra* extracts are more potent antioxidants, likely due to their richer phenolic profile

A study by Yuan *et al.* (2025) investigated the fermentation of whey protein (WP) and mulberry polyphenol (MP) adducts to improve protein digestibility. Using in vitro digestion models, the team analyzed proteolysis, antioxidant activity, and phenolic stability. Results showed WP-MP adducts increased proteolysis by 67% and retained 85% of anthocyanins during digestion. The adducts also enhanced antioxidant capacity (2.1-fold higher than WP alone) and modulated gut microbiota by promoting *Bifidobacterium* growth. LC-MS/MS revealed that WP protected MP from degradation, particularly cyanidin-3-glucoside. The study highlighted the potential of WP-MP complexes in functional foods for enhanced nutrient delivery

Tian *et al.* (2025) examined the therapeutic effects of mulberry fruit extract on high-fat diet (HFD)-induced male reproductive dysfunction in rodents. The study, published in *Nutrients*, involved administering standardized mulberry extract (anthocyanins: 2.92–5.35 mg/g) to HFD-fed mice for 28 days. Outcomes included increased antioxidant enzymes (SOD: +45%, catalase: +38%), reduced inflammation (TNF-α: −64%), and improved seminiferous tubule integrity (85% preservation). Molecular mechanisms involved AMPK/SIRT1 pathway activation and mitochondrial function enhancement. While promising, the study noted limitations like lack of human trials and standardized extraction protocols.

A study by Bian *et al.* (2025) analyzed anthocyanin synthesis in 'Hongguo No. 2' mulberry fruit and wine across five ripening stages. LC-MS/MS identified pelargonidin-3-O-glucoside as dominant in immature fruit, while cyanidin-3-O-rutinoside increased with maturity. Fermentation increased total phenols (1.8-fold) and anthocyanins (2.3-fold) in wine, with stage IV (black fruit) yielding the highest antioxidant activity. KEGG enrichment linked anthocyanin biosynthesis to phenylpropanoid pathways. The study recommended fully ripe fruit for wine production due to optimal sugar-acid balance and bioactive content.

James *et al.* (2024) reviewed mulberry leaf tea's effects on metabolic diseases, compiling evidence from preclinical and clinical studies. The review highlighted 1-deoxynojirimycin (DNJ) as a key α-glucosidase inhibitor, reducing postprandial glucose by 30% in diabetic patients. Mulberry leaf extracts also lowered LDL cholesterol (−24%) and uric acid (−18%) in human trials. The authors emphasized the need for standardized dosing but noted no adverse effects in 12-week trials. The study proposed mulberry leaf as a functional food for managing obesity and diabetes,

A study by Li *et al.,* (2021) summarized white mulberry's nutrient profile and health benefits. Fresh berries provided 51 mg vitamin C and 2.5 mg iron per cup (140 g), with dried forms offering higher protein (12%). Human trials showed mulberry leaf extract (1,000 mg/day) reduced HbA1c by 0.8% in diabetics. Test-tube studies noted anthocyanin-induced apoptosis in breast and colon cancer cells, though clinical evidence remained limited. The study concluded that mulberry's benefits for blood sugar and cholesterol warrant further human research. In 2025, a metabolomics and transcriptomics study explored ultrasound (US) elicitation to boost 1-DNJ and polyphenols in mulberry leaves. Using Box-Behnken design, optimal US conditions increased 1-DNJ (2.1-fold), total phenolics (2.7-fold), and flavonoids (2.1-fold). US-treated leaves showed higher α-glucosidase inhibition (85%) and upregulated genes in shikimate and phenylpropanoid pathways. The study proposed US as a green method to enhance mulberry leaves' nutraceutical value

| Health Benefit | Active Compounds | Source | Mechanism of Action | Evidence Type | References |
|---|---|---|---|---|---|
| **Antioxidant** | Anthocyanins, flavonoids, vitamin C, phenolic acids, tannins | Fruit, Leaf | Scavenges ROS; enhances antioxidant enzymes (SOD, CAT, GSH-Px); reduces lipid peroxidation; stabilizes free radicals | In vitro, In vivo | Chen *et al.,* (2015) |
| **Anti-diabetic** | DNJ, Fagomine, Anthocyanins, Flavonols, Polysaccharides | Leaf, Fruit | Inhibits α-glucosidase; enhances insulin sensitivity; modulates GLUT4, reduces gluconeogenesis, protects pancreatic β-cells, increases insulin secretion | In vitro, In vivo | Chen *et al.,* (2016a) |
| **Anti-obesity** | Anthocyanins, polyphenols, fiber | Leaf, Fruit | Reduces serum TC, TG, LDL; increases HDL; suppresses lipid accumulation; inhibits adipogenesis; activates hepatic enzymes for β-oxidation | Animal models, Human trial | Lim *et al.,* (2013). |
| **Anti-atherosclerosis** | Cyanidin-3-O-glucoside, protocatechuic acid, rutin, caffeic acid | Fruit | Inhibits LDL oxidation; reduces plaque formation; improves endothelial function; increases nitric oxide bioavailability | In vivo, Human | Onnom *et al.,* (2020) |
| **Neuroprotective** | Resveratrol, Cyanidin-3-O-glucoside, flavonols (quercetin, kaempferol) | Fruit | Inhibits AChE, BChE, BACE-1; reduces β-amyloid aggregation; suppresses neuroinflammation; improves synaptic function and reduces apoptosis | In vitro, In vivo | Strathearn *et al.,* (2014) |
| **Anti-cancer** | Anthocyanins, flavonoids, stilbenes, polyphenols | Fruit | Induces apoptosis in tumor cells; inhibits angiogenesis and metastasis; enhances NK and T-cell activity; suppresses tumor xenografts | In vitro, In vivo | Khalid *et al.,* (2017) |
| **Hepatoprotective** | Flavonoids, phenolics, polysaccharides | Fruit, Leaf | Reduces ALT, AST; boosts GSH, CAT, SOD; repairs liver tissue; prevents lipid accumulation and oxidative stress | Animal models | Zhao *et al.,* (2017) |
| **Anti-inflammatory** | Anthocyanins, quercetin, pyrrole alkaloids | Fruit | Inhibits COX-1/COX-2, TNF-α, IL-1β, iNOS, NF-κB pathway; reduces pro-inflammatory cytokines and | In vivo, In vitro | Xu *et al.,* (2020) |

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|---|---|---|---|---|---|
| | | | prostaglandins | | |
| **Immunomodulatory** | Pyrrole alkaloids, glycoproteins, polysaccharides | Fruit | Enhances macrophage phagocytosis; stimulates cytokine production (IL-12, TNF-α); promotes B-cell and T-cell proliferation | In vitro | Lim *et al.,* (2019) |
| **Anti-microbial** | Phenolics, flavonoids, alkaloids | Juice, Fruit | Inhibits growth of Gram-positive and Gram-negative bacteria (*E. coli*, *S. aureus*, *P. aeruginosa*); alters cell membranes | In vitro | Chen *et al.,* (2019) |
| **Anti-aging** | Polyphenols (resveratrol, quercetin), anthocyanins, vitamins | Leaf, Fruit | Delays oxidative damage; enhances SIRT expression; protects telomeres; boosts longevity genes (SOD-3, DAF-16 in *C. elegans*) | In vitro, Animal model | Gu *et al.,* (2017) |
| **Cardioprotective** | Linoleic acid, flavonoids, anthocyanins | Fruit | Regulates blood lipids; inhibits angiotensin activity; enhances nitric oxide production; improves endothelial cell survival | In vivo, Human | Rohela *et al.,* (2020) |
| **Anti-hypertensive** | Potassium, polyphenols | Fruit | Vasodilatory effect via nitric oxide modulation; reduces angiotensin-II levels | In vivo | He *et al.,* (2020) |
| **Vision Improvement** | β-Carotene, anthocyanins | Fruit | Protects retinal cells from oxidative damage; supports rhodopsin regeneration and retinal sensitivity | In vitro, Traditional use | Wen *et al.,* (2019) |
| **Gut Health** | Dietary fiber, polyphenols | Fruit | Improves bowel motility; relieves constipation; modulates microbiota; increases SCFA production | In vitro, Human | Jiang *et al.,* (2013) |
| **Anti-stress** | Antioxidants, flavonoids | Leaf, Fruit | Reduces oxidative markers in brain; modulates neurotransmitter levels; improves behavioral response | Animal models | Nade et al (2020) |
| **Sleep Support** | Melatonin | Fruit (wine) | Improves circadian rhythm and sleep onset; increases serum melatonin levels | Animal and Human | Lee *et al.,* (2016) |

**Table 5: Health benefits of mulberry and their mechanism of action**

**Extraction Techniques for Mulberry Extract and Their Food Industry Applications:**

The table below summarizes some extraction techniques used to retrieve bioactive compounds from mulberry (Morus spp.) as well as their usage in the food industry. Extraction is critical to the production of functional ingredients like antioxidants, colorants, and nutraceuticals which are increasingly gaining traction in health-conscious food products.

**Table 6: Extraction Techniques for Mulberry Extract and Their Food Industry Applications**

| Extraction Technique | Key Features | Advantages | Food Industry Applications | References |
|---|---|---|---|---|
| **Solvent Extraction** | Utilizes solvents like ethanol, methanol, or water to extract bioactive compounds from mulberry. | Simple, cost-effective, and widely used. | Production of natural colorants, flavor enhancers, and functional food ingredients. | Saini *et al.,* (2023) |
| **Ultrasound-Assisted Extraction (UAE)** | Employs ultrasonic waves to disrupt cell walls, enhancing the release of bioactives. | Increases extraction efficiency, reduces solvent usage, and shortens extraction time. | Extraction of phenolics and flavonoids for use in functional foods and beverages. | Martins *et al.,* (2023) |
| **Microwave-Assisted Extraction (MAE)** | Uses microwave energy to heat solvents and plant materials, facilitating compound release. | Rapid extraction with high yields and reduced solvent consumption. | Isolation of antioxidants and colorants for incorporation into health-oriented food products. | Jan *et al.,* (2021); Maqsood *et al.,* (2023) |
| **Supercritical Fluid Extraction (SFE)** | Utilizes supercritical $CO_2$ to extract compounds under specific temperature and pressure conditions. | Produces solvent-free extracts with high purity and selectivity. | Development of clean-label food additives and nutraceutical ingredients. | Yigit *et al.,* (2010); Khadivi *et al.,* (2024) |
| **Enzyme-Assisted Extraction (EAE)** | Applies enzymes like pectinase to degrade cell walls, enhancing compound release. | Environmentally friendly, improves yield, and preserves compound integrity. | Extraction of anthocyanins and polyphenols for use in natural food colorants and supplements. | Yang *et al.,* (2023) |
| **Natural Deep** | Combines | Green solvent | Isolation of | Hassan *et al.,* |

| | | | | |
|---|---|---|---|---|
| **Eutectic Solvent (NADES)-Based UAE** | NADES with ultrasound to extract bioactives efficiently. | system, customizable, and enhances extraction of specific compounds. | phenolics and flavonoids for functional food formulations. | (2020) |

## RECOMMENDATIONS

- To maintain good quality and effects for mulberry-based products, developing standard methods to obtain anthocyanins, flavonoids and polysaccharides is necessary. Ultrasound-assisted extraction (UAE), enzyme-assisted extraction (EAE) and high-speed shear homogenization require further study and adjustments for commercial use.
- We should study microencapsulation further and apply it to help the shelf life, stability and directed transport of mulberry's beneficial compounds in nutraceuticals and foods.
- The food industry might benefit by adding mulberry extracts to beverages, yogurts, protein bars and supplements that can help manage such conditions as diabetes, stress from oxidation and heart health.
- Further research should concentrate on using the nutritious mulberry seeds and leaves which are used much less than other parts. Their high level of protein, fiber and phenolic compounds suggests they are good for your health.
- The benefits observed in tests on mice and in test tubes need to be proven in people with chronic diseases such as diabetes, obesity and conditions where brain cells die.
- Scientists should use transcriptomics and metabolomics when breeding mulberry varieties that produce a lot of targeted beneficial plant compounds.
- Health benefits of mulberry need to be highlighted in both public campaigns and product labeling to help boost its sale and benefit the producers.
- Investing in mulberry farming, mainly in areas that get little rain, can help the environment, local economies and create income opportunities

## CONCLUSION

Mulberry (*Morus spp*.), including *M. alba, M. nigra* and *M. rubra*, is known for its impressive nutritional value, medicinal uses and a range of functions. The anthocyanins, phenolic acids, flavonoids, vitamins and minerals found in mulberries provide many health perks, including helping against oxidative damage, inflammation, diabetes, heart disease, brain disease and cancer. Even though mulberry seems very good for food applications, its usage in commercial products is not as high as it could be because of its high moisture, quick spoilage, unestablished extraction methods and low knowledge about its useful qualities. This review outlines how advanced ways of extracting and processing mulberry which use enzymes and various forms of waves and fast homogenizers, improve the quantity, stability and accessibility of mulberry's beneficial compounds. These methods help improve the usefulness, nutrition and storage time of products made from mulberries, making them useful in multiple food and nutraceutical applications.

The suitability of mulberry for use in functional foods and dietary supplements has been established through a variety of lab, animal and small human studies. Applying different approaches like whey protein fermentation, using ultrasound and encapsulation seems effective in protecting and boosting the delivery of its useful materials. In sum, mulberry is a fruit crop that is rarely used but has a lot of health-promoting properties. Efforts in the future should be directed toward sustainable ways to grow them, standardizing methods for making the extract and designing experiments to test their usefulness in medicines. As food science grows, mulberry can be a major ingredient in health-focused items, giving people natural options for handling diseases linked to lifestyle and improving how they feel generally

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