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Tamana Saini
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Punjab, India

Dr. Shweta Sharma
Assistant Professor, Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Phagwara, (Punjab) India

Harshpreet Singh
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Punjab, India

Poonam Jaglan
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Punjab, India

Corresponding Author:
Tamana Saini
Department of Food Technology and Nutrition, School of Agriculture, Lovely Professional University, Punjab, India

Exploring the nutritional and medicinal benefits of mulberry leaf: A comprehensive review

Tamana Saini, Dr. Shweta Sharma, Harshpreet Singh and Poonam Jaglan

Abstract
Mulberry leaves have been used in traditional medicine and cooking in different parts of the world for centuries. They are a rich source of vitamins, minerals, fiber, and protein. In addition, mulberry leaves contain bioactive compounds such as 1-deoxynojirimycin (DNJ), flavonoids, alkaloids, and polysaccharides. These compounds have various health benefits and are used in traditional medicine to treat various ailments. DNJ's hypoglycemic action helps regulate blood sugar levels. To make mulberry leaves useful dietary supplements for diabetics. Antioxidant and anti-inflammatory properties of anti-cancer, anti-diabetic, anti-hypertensive, anti-nociceptive, anti-aging, anti-anemic, and antibacterial flavonoids in mulberry leaves help prevent and treat chronic diseases such as cardiovascular disease. This review focuses on the nutritional and medicinal benefits of mulberry leaves and the potential therapeutic uses of their bioactive compounds.

Keywords: Antioxidant activity, bioactive compounds, cardiac function, functional food, mulberry leaves

Introduction
Mulberry leaves are known as *Morus spp* and belong to the Moraceae family. The mulberry tree is native to China, but has been cultivated all over the world for centuries, especially its leaves, which have been used for a variety of purposes. It has been used traditionally in traditional Japanese, Ayurvedic and Korean medicine. They have long been used to treat colds, diabetes and other ailments (Wen *et al*., 2019) [33]. Mulberry leaves are a rich source of various nutrients, including vitamins, minerals, protein, carbohydrates and dietary fiber, as well as bioactive compounds, including flavonoids, alkaloids, and polysaccharides. The nutritional value of mulberry leaves has been recognized for centuries, with ancient Chinese medicine using them to treat several ailments, including fever, cough, and respiratory infections. Additionally, mulberry leaves have been used in traditional Japanese medicine to treat diabetes and high blood pressure (Peanparkdee *et al*., 2016) [24].
In recent years, research has focused on the health-promoting effects of mulberry leaves, particularly their bioactive compounds including phenolic acids, flavonoids, alka-loids, andγ-aminobutyric acid (GABA). Studies have shown that mulberry leaves have hypoglycemic, antioxidant, anti-inflammatory, and immunomodulatory properties, among other benefits (Li *et al*., 2018) [16]. These properties make them potentially useful in the prevention and management of chronic diseases such as diabetes, cardiovascular disease, and cancer. The hypoglycemic effect of mulberry leaves is due to the presence of 1-deoxynojirimycin (DNJ), an alkaloid that inhibits alpha-glucosidase, an enzyme responsible for the breakdown of carbohydrates into simple sugars. By inhibiting this enzyme, mulberry leaves slow down the absorption of glucose into the bloodstream, which helps regulate blood sugar levels (Kojima *et al*., 2010) [14].
The use of medicinal plants is still significant in rising and developing nations. One of the significant traditional herbs that have been utilized for decades in medicine is the mulberry plant. It contains a high amount of nutrients and phytochemical substances and has a variety of therapeutic benefits (Tchabo *et al*., 2022) [28]. It also contains a lot of flavonoids and other substances with potential antibacterial effects as well as free radical scavenging abilities. All components of the plant are utilized as a medication because of its pharmacological qualities. Mulberry has been shown to protect the liver, enhance vision, and make it easier for people to pass urine, lower blood pressure, and lower cholesterol, strengthen bone structures, and improve immunity (Wani *et al*., 2023) [30].

Overall, mulberry leaves have been found to have various health benefits, making them a promising source of natural remedies for several ailments. This comprehensive review aims to explore the nutritional and medicinal benefits of mulberry leaves, with a particular focus on their bioactive compounds. The review will also discuss the potential uses of mulberry leaf extracts as dietary supplements and in the development of new therapeutics for various health conditions.

Bioactive composition of mulberry leaves

The bioactive compounds found in mulberry leaves are of great importance due to their potential health benefits. Flavonoids and phenolic acids are powerful antioxidants that may help protect the body from oxidative stress and inflammation, which are known to contribute to the development of chronic disease. Alkaloids and glycosides in mulberry leaves can also have various physiological effects that may be beneficial to human health, such as: lowering blood sugar levels (Bai *et al*., 2023) [2]. In addition, mulberry leaves are a good source of vitamins and minerals that are essential for overall health and well-being. The bioactive compounds in mulberry leaves thus make them a valuable ingredient in functional foods and dietary supplements aimed at promoting health and preventing chronic diseases (Dhiman *et al*., 2020) [6].

- **Phenolics:** Mulberry leaves are a rich source of phenolic compounds, which are a type of antioxidant that have been extensively studied for their potential health benefits. Chlorogenic acid is the most abundant phenolic compound found in mulberry leaves and has been shown to have anti-inflammatory, anti-cancer, and anti-obesity properties (Zou *et al*, 2012) [38]. Other phenols found in mulberry leaves, such as gallic acid, and caffeic acid, also have various health benefits, including antioxidant, anti-inflammatory, and anti-cancer effects. The presence of these phenolic compounds in mulberry leaves makes them a valuable ingredient in functional foods and dietary supplements aimed at promoting health and preventing chronic diseases (Liao *et al*., 2021).
- **Flavonoids:** Mulberry leaves are also high in flavonoids, a type of antioxidant that has been extensively studied for its potential health benefits. Flavonoids found in mulberry leaves include rutin, quercetin, kaempferol, and morin. These flavonoids have been shown to have anti-inflammatory, anti-cancer and anti-diabetic properties (Wen *et al*, 2021) [32]. For example, rutin has been found to help lower blood sugar levels and improve insulin sensitivity, making it potentially beneficial for people with diabetes. Quercetin has been shown to have anti-inflammatory effects and may reduce the risk of chronic diseases such as cardiovascular disease and cancer. The presence of these flavonoids in mulberry leaves makes them a valuable source of these important bioactive compounds with potential health benefits for human health (He *et al*., 2013) [9].
- **Alkaloids:** Mulberry leaves contain various alkaloids, a type of organic compound that can have physiological effects on the human body. Some of the alkaloids found in mulberry leaves include kuwanon, kuwanon G, and mulberrofuran G. These alkaloids have been shown to have various health benefits, including anti-inflammatory and antitumor properties (Ji *et al*., 2016) [13]. They may also have potential therapeutic effects on conditions like diabetes, as some studies have found they can help lower blood sugar levels and improve insulin sensitivity. The presence of these alkaloids in mulberry leaves makes them a valuable source of these important bioactive compounds with potential health benefits for human health (Guo *et al*., 2019) [8].

Function of different bioactive compounds

- **Chlorogenic acid:** Chlorogenic acid is the most abundant phenolic compound found in mulberry leaves. It is a powerful antioxidant that has been shown to have various health benefits. Chlorogenic acid has been found to have anti-inflammatory properties that may be beneficial in reducing the risk of chronic diseases such as cardiovascular disease and diabetes. It has also been shown to have anti-cancer properties, with studies suggesting that it may help prevent cancer cells from growing and spreading (Hunyadi *et al*., 2012) [11]. In addition, chlorogenic acid has been shown to have anti-obesity effects and may help regulate metabolism and reduce body weight. Chlorogenic acid has also been found to have neuroprotective effects that may help prevent age-related cognitive decline. Overall, the presence of chlorogenic acid in mulberry leaves makes them a valuable source of this important phenolic compound with potential health benefits for human health (Zhai *et al*., 2018) [36].
- **Gallic acid:** Gallic acid is a type of polyphenol compound found in mulberry leaves. It is also found in various other plant foods such as grapes, tea and berries. Known for its antioxidant and anti-inflammatory properties, gallic acid has been studied for its potential health benefits. Studies have shown that gallic acid in mulberry leaves may help protect against oxidative stress and inflammation, which can contribute to the development of chronic diseases (He *et al*., 2020) [10]. In addition, gallic acid may have antimicrobial and anti-cancer properties. A study published in the Journal of Agricultural and Food Chemistry found that gallic acid in mulberry leaves had a significant inhibitory effect on cancer cell growth. Another study suggested that gallic acid in mulberry leaves may have potential as a natural antimicrobial against various types of bacteria (Ge *et al*., 2018) [7].
- **Caffiec acid:** Caffeic acid is a type of phenolic acid found in mulberry leaves. It is a powerful antioxidant and has numerous health benefits. Studies have shown that caffeic acid has anti-inflammatory and anti-cancer properties. It may also have potential therapeutic effects on conditions such as cardiovascular disease and diabetes (Wanyo *et al*., 2011) [31]. Additionally, caffeic acid has been found to have antimicrobial and antiviral properties, making it potentially beneficial for fighting infections. The presence of caffeic acid in mulberry leaves makes them a valuable source of this important phenolic compound with potential health benefits for human health (Tajner-Czopek *et al*., 2020).
- **Rutin:** Rutin is a type of flavonoid found in mulberry leaves. It is a powerful antioxidant and has numerous health benefits. Studies have shown that rutin has anti-inflammatory and anti-cancer properties. It may also have potential therapeutic effects on conditions such as

cardiovascular disease and diabetes (Ou-yang *et al*., 2013) [22]. Additionally, rutin has been found to have anti-allergic and anti-viral properties, making it potentially beneficial for fighting allergies and viral infections. The presence of rutin in mulberry leaves makes them a valuable source of this important flavonoid with potential health benefits for human health (Kim *et al*., 2014).

- **Quercetin:** Quercetin is another flavonoid compound found in mulberry leaves. It is a natural pigment that gives plants, fruits and vegetables their color. Quercetin has been extensively studied for its potential health benefits, including antioxidant, anti-inflammatory, and anti-cancer properties. Mulberry leaves have been found to contain significant amounts of quercetin, and studies suggest that consuming mulberry leaves or extracts may provide health benefits (Ou-yang *et al*., 2013) [22]. Research has shown that quercetin in mulberry leaves may help reduce inflammation, regulate blood sugar levels, and support cardiovascular health. A study published in the Journal of Agricultural and Food Chemistry found that quercetin in mulberry leaves may help reduce oxidative stress and inflammation in the body and may help prevent chronic diseases like cancer and heart disease. Another study suggested that quercetin in mulberry leaves may help regulate blood sugar levels by increasing insulin sensitivity and improving glucose metabolism (Enkhmaa *et al*., 2005).
- **Kaempferol:** Kaempferol is a type of flavonoid found in mulberry leaves. It is a powerful antioxidant and has numerous health benefits. Studies have shown that kaempferol has anti-inflammatory and anti-cancer properties. It may also have potential therapeutic effects on conditions such as cardiovascular disease and diabetes (Lee *et al*., 2015) [15]. Additionally, kaempferol has been found to have neuroprotective effects and may help prevent age-related cognitive decline. The presence of kaempferol in mulberry leaves makes them a valuable source of this important flavonoid with potential health benefits for human health (Ju *et al*., 2018).
- **Morin:** Morin is a flavonoid compound found in various plants including mulberry leaves. Mulberry leaves are a natural source of morin and have been used in traditional medicine for their potential health benefits. Morin has been studied for its antioxidant, anti-inflammatory, and anti-cancer properties (Zhang *et al*., 2018) [37]. It has been found to have a number of potential health benefits including protecting against oxidative stress and inflammation, promoting healthy blood sugar levels and supporting cardiovascular health. Research has shown that morin in mulberry leaves may have potential therapeutic uses in treating various health conditions, including diabetes, cancer, and cardiovascular disease (Rison *et al*., 2020) [25].

Health benefits of mulberry leaves

- **Lower blood sugar:** 1-Deoxynojirimycin (DNJ) is a compound found in mulberry leaves that has been shown to inhibit alpha-glucosidase, an enzyme that breaks down carbohydrates into glucose. By inhibiting this enzyme, DNJ can slow the digestion and absorption of carbohydrates, which helps prevent blood sugar spikes. Mulberry leaves also contain several flavonoids, including quercetin and kaempferol, which have been shown to have anti-diabetic properties (Sarkhel *et al*., 2020) [26]. These compounds may help improve insulin sensitivity and regulate blood sugar levels. Mulberry leaves contain gamma-aminobutyric acid (GABA), an amino acid that has been shown to improve glucose metabolism and insulin sensitivity. Studies have found that mulberry leaf extract may help lower blood sugar levels in people with type 2 diabetes. For example, a 2016 study published in the Journal of Functional Foods found that taking 280 mg of mulberry leaf extract three times a day for four weeks resulted in a significant reduction in fasting blood glucose levels, HbA1c levels a measure of long-term blood glucose control and insulin resistance in people with type 2 diabetes (Xasanova., 2022) [34].
- **Anti-inflammation:** Quercetin is a flavonoid found in mulberry leaves that has been shown to have potent anti-inflammatory effects. It works by inhibiting the production of inflammatory cytokines, which are molecules that contribute to inflammation. Morin is another flavonoid found in mulberry leaves that has been shown to have anti-inflammatory properties. It works by inhibiting the activation of NF-kB, a protein complex that plays a key role in the inflammatory response. Chlorogenic acid is a phenolic acid found in mulberry leaves that has been shown to have anti-inflammatory properties (Park *et al*., 2013) [23]. It works by inhibiting the production of inflammatory cytokines and reducing oxidative stress. Studies have found that mulberry leaf extract can help reduce inflammation in different parts of the body. For example, a 2018 study published in the journal Nutrients found that taking 1,000 mg of mulberry leaf extract per day for eight weeks resulted in a significant reduction in inflammatory markers in people, with metabolic syndrome (Lim *et al*., 2013) [17].
- **Improve heart health:** Mulberry leaves contain compounds that may help relax blood vessels and improve blood flow, which may help lower blood pressure. High blood pressure is a major risk factor for heart disease, so lowering it can be beneficial for heart health. Mulberry leaves contain compounds called flavonoids, which have been shown to lower levels of LDL (bad) cholesterol and triglycerides in the blood (Cao *et al*., 2021) [3]. High LDL cholesterol can increase your risk of heart disease, so lowering it may be beneficial. Mulberry leaves are high in antioxidants, which may help protect the heart and blood vessels from free radical damage. Free radicals can contribute to the development of heart disease, so reducing their effects can be beneficial. Mulberry leaves contain compounds with anti-inflammatory properties that can help reduce inflammation in the body. Chronic inflammation can contribute to the development of heart disease, so reducing it may be beneficial (Thaipitakwong *et al*., 2018) [29].
- **Boost immune system:** Mulberry leaves are high in antioxidants, which can help protect the body from free radical damage. Free radicals can weaken the immune system, so reducing their effects can be beneficial. Mulberry leaves contain compounds with anti-inflammatory properties that can help reduce inflammation in the body (Neamat-Allah *et al*., 2021) [21]. Chronic inflammation can weaken the immune system,

so reducing it can be beneficial. Some studies suggest that mulberry leaves may help stimulate the production of white blood cells, which are important for immune function. Mulberry leaves contain compounds that may help promote the growth of beneficial bacteria in the gut that may help support immune function (Chen *et al*., 2021) [5].

- **Treat skin conditions:** Mulberry leaves are rich in polyphenols, antioxidants that protect skin from free radical damage. Free radicals can cause oxidative stress, which can lead to premature aging and other skin problems. Mulberry leaves also contain flavonoids, which have anti-inflammatory and antimicrobial properties. These properties can help reduce inflammation and prevent bacterial or fungal infections on the skin. Mulberry leaves are a good source of vitamin C, which is an essential nutrient for skin health (Sharma *et al*., 2020) [27]. Vitamin C helps boost collagen production, which can help improve skin elasticity and reduce the appearance of fine lines and wrinkles. Studies have found that topical application of mulberry leaf extract or powder can help improve various skin conditions such as acne, hyperpigmentation, and wrinkles. For example, a 2015 study published in the Journal of Drugs in Dermatology found that a cream containing mulberry extract and arbutin (another skin-lightening ingredient) significantly reduced the appearance of dark spots and hyperpigmentation in people with melisma (Nangare *et al*., 2021) [20].
- **Anticancer:** Mulberry leaves are rich in antioxidants, which can help protect cells from free radical damage. Free radicals can contribute to the development of cancer by damaging DNA and other cell structures. By neutralizing free radicals, antioxidants in mulberry leaves may help prevent or slow the growth of cancer cells. Apoptosis is a process of programmed cell death that occurs naturally in the body. Cancer cells are often resistant to apoptosis, which allows them to continue growing and dividing. However, studies have found that compounds in the mulberry leaf can induce apoptosis in cancer cells, which may help slow or stop their growth (Chan *et al*., 2020) [4]. Angiogenesis is the process by which new blood vessels are formed, which is necessary for the growth and spread of tumors. Studies have found that compounds in mulberry leaves can inhibit the formation of new blood vessels, which may help prevent cancer cells from growing and spreading. Cancer cells divide and grow out of control, leading to the development and spread of tumors. Studies have found that compounds in mulberry leaves can inhibit the proliferation of cancer cells, which may help slow or stop tumor growth (Bae & Ye., 2010) [1] (Fig 1).

Fig 1: Health benefits of mulberry leaves

Neuroprotective effect

Mulberry leaves contain several compounds that have been found to have potential neuroprotective effects. Mulberry leaves are high in antioxidants, which may help protect brain cells from free radical damage. Free radicals can contribute to the development of neurodegenerative diseases such as Alzheimer's and Parkinson's. By neutralizing free radicals, antioxidants in mulberry leaves may help prevent or slow the progression of these diseases. Chronic inflammation is thought to contribute to the development of neurodegenerative diseases. Mulberry leaves contain several compounds, including quercetin and morin, which have anti-inflammatory properties. These compounds may help reduce inflammation in the brain, which may be beneficial for those with neurodegenerative diseases (Wen *et al*., 2021) [32]. Some compounds in mulberry leaf have been found to have direct neuroprotective effects. For example, studies have found that mulberry leaf extract may help protect against neurotoxicity and improve cognitive function in animal models of Alzheimer's disease. Mulberry leaves contain compounds that may help modulate neurotransmitter levels in the brain. For example, one study found that a compound in mulberry leaves called 1-deoxynojirimycin (DNJ) can increase levels of acetylcholine, a neurotransmitter important for memory and learning (Mairuae *et al*., 2023) [18].

Food applications of mulberry leaves

One of the most common uses of mulberry leaves in food is as a tea. The leaves can be dried and steeped in hot water to make a flavorful and aromatic tea. Mulberry leaf tea is often consumed for its health benefits, including its potential to lower blood sugar levels and reduce inflammation. In some kitchens, mulberry leaves are used as a wrap for cooking food. For example, in Korean cuisine, gimbap is a dish in which rice and various fillings are wrapped in a sheet of dried mulberry leaves. Young mulberry leaves can be used as a nutritious and tasty ingredient in salads (Jan *et al*., 2021) [12]. The leaves can be blanched to soften them and remove any bitterness before adding them to a salad. Mulberry leaves can also be added to soups for flavor and nutrition. In Chinese cuisine, for example, mulberry leaves are often used in a soup with pork ribs and red dates. Dried mulberry leaves can be ground into a powder and used as a spice for various dishes. The powder has a slightly sweet and earthy taste and can be

used in marinades, rubs, and other condiments (Maqsood *et al*., 2022) [19] (Fig 2). Mulberry leaf extract is also available as a dietary supplement. These supplements are often marketed for their potential to lower blood sugar levels, reduce inflammation, and support overall health. The powder has a slightly sweet, earthy taste and can be used in marinades, labs, and other seasonings. In some parts of the world, mulberry leaf wine is made by fermenting mulberry leaves with sugar and yeast. The resulting wine has a sweet and fruity flavor and is often drunk as a traditional medicine. Mulberry leaf jam is a sweet and tangy spread made by boiling mulberry leaves with sugar and fruit. It is often used as a topping for bread, pancakes and other foods. In some parts of Asia, tofu is made with mulberry leaves. This type of tofu, often called "blue tofu," has a slightly grassy flavor (Yu *et al*., 2018) [35].

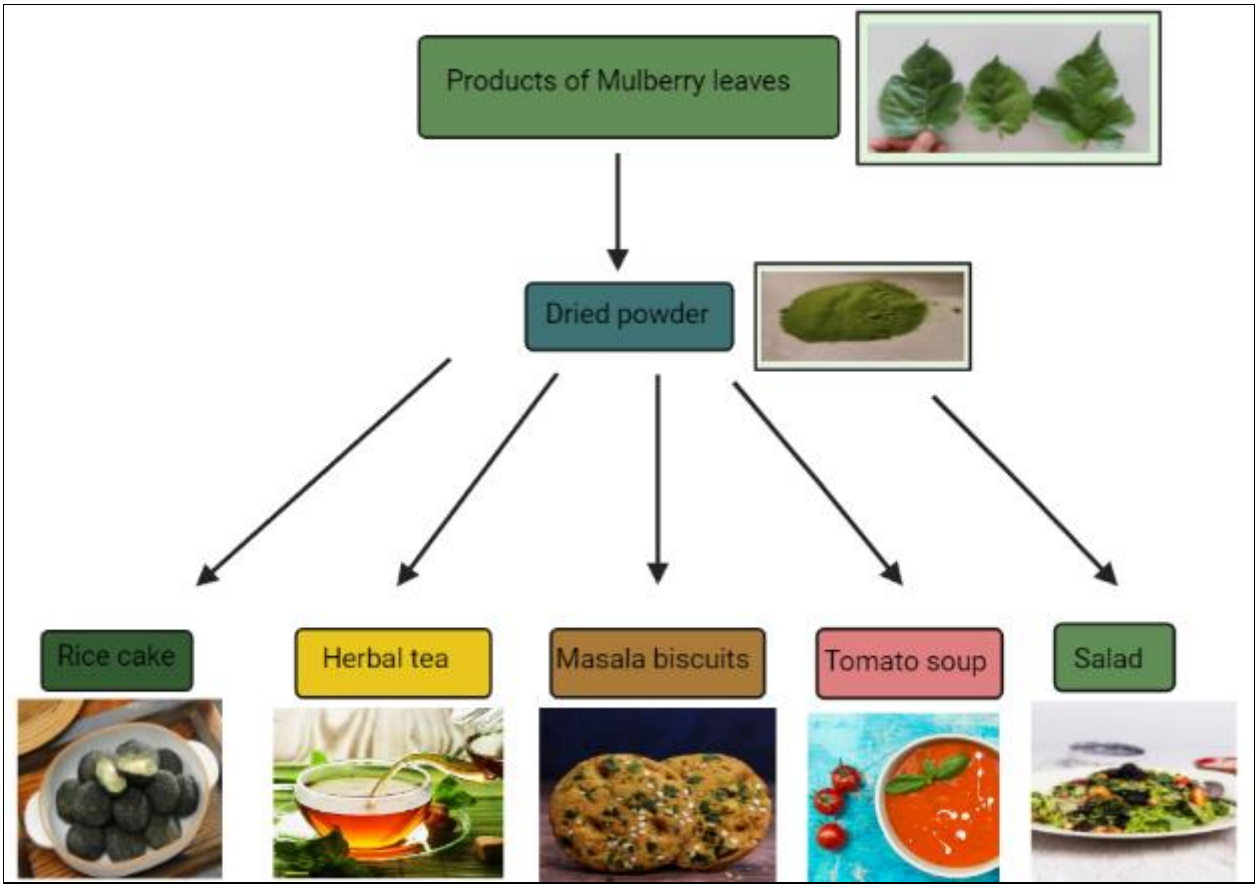

Fig 2: Different food applications of mulberry

Future perspective

Mulberry leaves contain many bioactive compounds with potential health benefits, including flavonoids, alkaloids, and polysaccharides. New functional foods and supplements may be developed to target the condition. Mulberry leaves are an important food source for silkworms, and the development of high-yielding mulberry cultivars has been the focus of research for many years. In the future, new mulberry varieties with improved yields and nutritional profiles may be developed, making them more sustainable and cost-effective for both sericulture and human consumption. Mulberry leaves are rich in nutrients and have been used as a natural fertilizer and soil conditioner in some agricultural systems. With growing interest in sustainable agriculture, mulberry leaves may be used more widely as a natural and renewable resource to improve soil quality and yields. has been shown to have the ability to absorb heavy metals from soil and water and may be useful in bioremediation. You can explore the possibilities of mulberry leaves.

Conclusion

In summary, mulberry leaf is a plant that has been used in traditional medicine for centuries for its many health benefits. Recent research has revealed its potential nutritional and medicinal benefits. It has become an area of growing interest in the scientific community. Mulberry leaves are rich in antioxidants, anti-inflammatory compounds, vitamins, minerals and flavonoids, and are used in a variety of Potential health benefits. Potential mulberry leaf benefits include improving heart health, strengthening the immune system, treating skin conditions, lowering blood sugar levels, and certain types of cancer. Mulberry leaves are also used in the food industry for their sweetness and nutritional value. Although more research is needed to fully understand the effects of mulberry leaf on human health, the available evidence suggests it could be a valuable addition to a healthy diet and lifestyle. Overall, mulberry leaf is a promising plant that deserves further research and investigation for its potential nutritional and medicinal benefits.

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