



Review Article : Open Access

Bioactive compounds in Mulberry (*Morus* spp.) and their products in curing human health problems: A comparative analysis

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Article Info

Article history

Received 3 September 2024

Revised 21 October 2024

Accepted 22 October 2024

Published Online 30 December 2024

Keywords

Applications

Bioactive compounds

Health benefits

Mulberry

Mulberry extract

Medicinal value

Abstract

Mulberry (*Morus* spp.) is not only vital for sericulture but also holds immense potential in human health due to its rich composition of bioactive compounds. The leaves, fruits, and other parts of the Mulberry plant are packed with a diverse range of bioactive components, including flavonoids, alkaloids, polyphenols, anthocyanins, and vitamins, which exhibit significant therapeutic properties. These compounds have been shown to possess antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer properties, thereby making Mulberry a promising functional food in the prevention and treatment of various human health problems. One of the most extensively studied bioactive compounds in Mulberry is 1-deoxynojirimycin (DNJ), which has strong antidiabetic properties. In addition, Mulberry extracts have been reported to enhance lipid metabolism, thus contributing to the prevention of cardiovascular diseases. The antioxidant properties of Mulberry are primarily attributed to its high content of phenolic compounds, which neutralize free radicals, reduce oxidative stress, and help in the management of ageing related diseases and certain cancers. Mulberry's anti-inflammatory and antimicrobial activities also make it effective in treating infections and chronic inflammatory conditions. Furthermore, Mulberry fruits and leaves have been utilized in traditional medicine for improving digestive health and managing neurological disorders. The bioactive compounds present in Mulberry and its derived products offer significant health benefits, thus suggesting their potential use in modern therapeutics and functional foods to address a wide range of human health challenges.

1. Introduction

Mulberry (*Morus* spp.), a tree native to Asia and has been an integral part of traditional medicine for centuries, renowned for its therapeutic properties across various cultures (Bharathi *et al.*, 2022). Its medicinal significance can be traced back to ancient civilizations, where it was used in the treatment of diverse ailments, from respiratory disorders to skin conditions (Chen *et al.*, 2021). Modern research has validated many of these traditional uses, thus attributing the plant's health benefits to a complex array of bioactive compounds (Verma *et al.*, 2022). This introduction explores the medicinal constituents of Mulberry, thereby examining their roles in human health and their potential in curing a range of health problems, with a particular focus on diabetes. Additionally, it compares the effectiveness of these compounds with those found in other plant extracts, thus highlighting the unique therapeutic advantages of Mulberry.

Mulberry's medicinal properties are primarily attributed to its rich composition of bioactive compounds, including flavonoids,

polyphenols, alkaloids, and sterols. These compounds have been extensively studied for their health benefits, particularly in managing chronic diseases such as diabetes, cardiovascular disorders, and inflammation (Ma *et al.*, 2022). One of the key bioactive constituents of Mulberry is 1-deoxynojirimycin (DNJ), a cyclic imino sugar known for its potent α -glucosidase inhibitory activity. DNJ's ability to inhibit this enzyme makes it highly effective in controlling postprandial blood glucose levels by slowing down the digestion and absorption of carbohydrates. This mechanism is particularly beneficial for individuals with type 2 diabetes, as it helps manage blood sugar spikes after meals (Rohela *et al.*, 2020).

In addition to DNJ, Mulberry contains several other bioactive compounds with significant therapeutic potential. Quercetin and kaempferol, two prominent flavonoids, were recognized for their powerful antioxidant and anti-inflammatory properties. Quercetin, with its hydroxylated benzopyrone structure, will scavenge free radicals and reduce oxidative stress, which is a critical factor in the development of diabetes-related complications (Wen *et al.*, 2019). Similarly, kaempferol is another flavonoid with a similar structure that contributes to antioxidant defense and enhances insulin sensitivity, thus supporting better glucose metabolism. Rutin, a flavonoid glycoside found in Mulberry, adds another layer of therapeutic benefit. It not only provides antioxidant protection but also supports vascular health by strengthening blood vessels and

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reducing inflammation (Zhumabavev *et al.*, 2021). Chlorogenic acid, a polyphenol present in Mulberry, is notable for its role in glucose metabolism. By reducing gluconeogenesis and promoting glucose uptake in peripheral tissues, chlorogenic acid helps regulate blood sugar levels and supports overall metabolic health. Another important bioactive compound in Mulberry is β -sitosterol, a phytosterol with a structure similar to cholesterol. β -sitosterol is known for its cholesterol-lowering effects, which are beneficial in managing cardiovascular health and metabolic syndrome. By competing with cholesterol for absorption in the intestines, β -sitosterol helps reduce blood cholesterol levels, thus mitigating the risk of heart disease and supporting metabolic health (Sanchez *et al.*, 2015). Gallic acid and ellagic acid, both polyphenolic compounds, further enhance the therapeutic profile of Mulberry. Ellagic acid, characterized by its two connected phenolic rings, provides potent antioxidant and anti-inflammatory effects, thereby contributing to better glycemic control and overall health improvement (Maqsood *et al.*, 2022).

In exploring the medicinal constituents of Mulberry, it is essential to compare their effectiveness with other plant-based treatments. Mulberry's unique combination of bioactive compounds offers a synergistic approach to managing health conditions, particularly diabetes (Kadam *et al.*, 2019). For instance, while many other plant extracts also contain antioxidants and anti-inflammatory agents, Mulberry's specific blend of DNJ, quercetin, kaempferol, rutin, chlorogenic acid, β -sitosterol, gallic acid, and ellagic acid provides a multifaceted mechanism of action that enhances its therapeutic efficacy. Comparative studies highlight that while other plants like cinnamon, fenugreek, and bitter melon also offer beneficial effects in diabetes management, Mulberry's diverse range of bioactive compounds and their synergistic interactions provide a distinctive advantage (Kishore and Kumar, 2020). For example, while cinnamon and fenugreek contain compounds with glucose-lowering properties, the unique α -glucosidase inhibitory effect of DNJ in Mulberry provides a specific and potent mechanism for controlling postprandial blood glucose levels (Singh *et al.*, 2022). Similarly, the comprehensive antioxidant and anti-inflammatory effects of Mulberry's flavonoids and polyphenols offer a broader range of therapeutic benefits compared to other plant extracts (Afzal *et al.*, 2021).

The integration of Mulberry's medicinal properties into contemporary therapeutic practices holds significant promise. Its traditional uses and modern scientific validation make it a compelling candidate for inclusion in dietary supplements and functional foods aimed at managing chronic diseases (Bhattachariya *et al.*, 2021). By harnessing the full potential of Mulberry's bioactive constituents, researchers and healthcare practitioners can develop more effective strategies for preventing and managing health conditions such as diabetes, cardiovascular diseases, and inflammation (Mehrotra *et al.*, 2021). Mulberry stands out as a plant with substantial medicinal value with a rich array of bioactive compounds. The key constituents, including DNJ, quercetin, kaempferol, rutin, chlorogenic acid, β -sitosterol, gallic acid, resveratrol, and ellagic acid, each contribute to its therapeutic efficacy through various mechanisms such as enzyme inhibition, antioxidant defence, and anti-inflammatory effects (Chen *et al.*, 2022). Comparative studies with other plant extracts underscore Mulberry's unique advantages and its potential role in modern medicine (Choi *et al.*, 2012). As research continues to uncover the full range of Mulberry's health benefits, it is poised to become an important component of integrative approaches to managing chronic

health conditions and enhancing overall wellbeing (Bharathi *et al.*, 2024).

2. Medicinally important bioactive compounds in Mulberry

Mulberry is known to contain a diverse array of bioactive compounds, each contributing uniquely to its medicinal properties were listed in Table 1. The most important compounds include 1-deoxynojirimycin (DNJ), quercetin, kaempferol, rutin, chlorogenic acid, β -sitosterol, gallic acid, resveratrol, and ellagic acid. Each of these compounds has been investigated for its potential health benefits, especially in the context of metabolic disorders such as diabetes (Khalifa *et al.*, 2018).

2.1 1-deoxynojirimycin (DNJ)

1-deoxynojirimycin (DNJ) is a cyclic imino sugar that has garnered significant attention due to its potent α -glucosidase inhibitory activity. The chemical structure of DNJ includes a five-membered cyclic ring with an imino group and multiple hydroxyl groups, which are crucial for its enzymatic inhibition. DNJ's primary mechanism of action is its ability to inhibit α -glucosidase, an enzyme responsible for the breakdown of complex carbohydrates into glucose in the digestive tract (Ai *et al.*, 2021). By inhibiting this enzyme, DNJ slows down the absorption of glucose, thereby reducing postprandial blood glucose levels (Bilawal *et al.*, 2021). This mechanism is particularly beneficial for managing type 2 diabetes, as it helps in controlling blood sugar spikes after meals. Clinical studies have demonstrated that DNJ can effectively lower blood glucose levels and improve glycemic control in individuals with diabetes (Fatima *et al.*, 2024). Additionally, it may help in reducing the risk of long-term complications associated with diabetes by maintaining stable blood sugar levels (Dhiman *et al.*, 2020).

2.2 Quercetin

Quercetin is a flavonoid characterized by its benzopyrone backbone and multiple hydroxyl groups. Its structure contributes to its potent antioxidant and anti-inflammatory properties. Quercetin is widely distributed in various fruits, vegetables, and plants, thus including Mulberry. Quercetin exerts its effects through several mechanisms. As a powerful antioxidant, it scavenges free radicals and reduces oxidative stress, which is a significant factor in the development of diabetes-related complications (Jan *et al.*, 2021). Additionally, quercetin modulates inflammatory pathways, thus reducing systemic inflammation and improving insulin sensitivity. The antioxidant and anti-inflammatory effects of quercetin contribute to better overall metabolic health. Research indicates that quercetin supplementation can improve insulin sensitivity, reduce blood glucose levels, and mitigate inflammation associated with diabetes and cardiovascular diseases (D'urso *et al.*, 2019).

2.3 Kaempferol

Kaempferol is another important flavonoid found in Mulberry with a structure similar to quercetin but with fewer hydroxyl groups. Its chemical formula includes a benzopyrone ring with hydroxyl substitutions. Kaempferol functions primarily through its antioxidant activity. It neutralizes reactive oxygen species (ROS) and protects cells from oxidative damage (Gomez *et al.*, 2021). Furthermore, kaempferol promotes glucose uptake in cells and enhances insulin sensitivity, thus aiding in more effective blood glucose management. Kaempferol's antioxidant properties help reduce oxidative stress and inflammation, which are key factors in the progression of diabetes.

By improving insulin sensitivity and glucose metabolism, kaempferol supports overall metabolic health and helps manage diabetes effectively (Yuan and Zhao, 2017).

2.4 Rutin

Rutin is a flavonoid glycoside made up of quercetin connected to a rutinose sugar component. Its chemical structure includes a flavonoid backbone with a sugar attachment, which influences its bioavailability and activity. Rutin exhibits a range of biological activities including

antioxidant, anti-inflammatory, and vasoprotective effects. It helps reduce oxidative stress, stabilize blood vessels, and decrease inflammation (Marchetti *et al.*, 2022). Additionally, rutin has been shown to enhance insulin sensitivity and regulate blood glucose levels. The combined antioxidant and anti-inflammatory properties of rutin contribute to improved metabolic health and reduced risk of cardiovascular complications. Rutin supplementation may aid in managing diabetes by enhancing glucose metabolism and providing cardiovascular protection (Memete *et al.*, 2021).

Table 1: Medicinal important bioactive compounds in Mulberry with percentage amounts

Bioactive compound	Chemical formula	Functions	Benefits	References
1-deoxynojirimycin (DNJ)	$C_6H_{13}NO_4$	Inhibits α -glucosidase, reducing glucose absorption in the intestines.	Key compound for lowering blood glucose levels.	Ramappa <i>et al.</i> , 2020
Quercetin	$C_{15}H_{10}O_7$	Antioxidant, anti-inflammatory, improves insulin sensitivity.	Prominent flavonoid with various health benefits.	Lin <i>et al.</i> , 2020
Kaempferol	$C_{15}H_{10}O_6$	Antioxidant, reduces oxidative stress, and improves blood glucose regulation.	Contributes to overall metabolic health.	Ju <i>et al.</i> , 2018
Rutin	$C_{27}H_{30}O_{16}$	Antioxidant, strengthens blood vessels, and reduces inflammation.	Works synergistically with other flavonoids.	Wen <i>et al.</i> , 2019
Chlorogenic acid	$C_{16}H_{18}O_9$	Antioxidant, modulates glucose metabolism and has anti-inflammatory effects.	Also found in coffee; helps regulate blood sugar levels.	Liu <i>et al.</i> , 2019
β -sitosterol	$C_{29}H_{50}O$	Phytosterol that can help lower cholesterol and may support cardiovascular health.	Provides additional benefits related to heart health.	Chen <i>et al.</i> , 2020
Gallic acid	$C_7H_6O_5$	Antioxidant, anti-inflammatory, and has potential antidiabetic effects.	Contributes to the antioxidant profile of Mulberry.	Gundogdu <i>et al.</i> , 2017
Resveratrol	$C_{14}H_{12}O_3$	Antioxidant, supports metabolic health and has potential antidiabetic properties.	Found in small amounts; adds to the overall health benefits.	Li <i>et al.</i> , 2021
Ellagic acid	$C_{14}H_6O_8$	Antioxidant, may help reduce oxidative stress and inflammation.	Provides additional antioxidant support.	Natic <i>et al.</i> , 2015

2.5 Chlorogenic acid

Chlorogenic acid is a phenolic compound formed by the esterification of caffeic acid and quinic acid. Its structure consists of a caffeic acid moiety linked to a quinic acid ring. Chlorogenic acid impacts glucose metabolism by inhibiting glucose-6-phosphatase, an enzyme involved in gluconeogenesis. This action reduces glucose production in the liver and promotes glucose uptake in cells (Polumackanycz *et al.*, 2019). Additionally, chlorogenic acid has antioxidant and anti-inflammatory effects. Studies suggest that chlorogenic acid can help lower blood glucose levels, improve insulin sensitivity, and support weight management. Its multifaceted effects make it a valuable compound for managing diabetes and enhancing metabolic health (Saeed *et al.*, 2023).

2.6 β -sitosterol

β -sitosterol is a phytosterol with a chemical structure similar to cholesterol but with a distinct side chain. It is commonly found in various plant-based foods, including Mulberry. β -sitosterol lowers blood cholesterol levels by competing with cholesterol for absorption

in the intestines. This leads to reduced cholesterol levels in the bloodstream (Teodoro *et al.*, 2019). Additionally, β -sitosterol has anti-inflammatory effects that support overall cardiovascular health. The cholesterol lowering effects of β -sitosterol contribute to improved cardiovascular health. By reducing LDL cholesterol levels, β -sitosterol helps decrease the risk of heart disease and supports better metabolic health (Dimitrijevic *et al.*, 2021).

2.7 Gallic acid

Gallic acid is a trihydroxybenzoic acid with a chemical structure that includes three hydroxyl groups attached to a benzoic acid ring. Gallic acid functions primarily as an antioxidant, scavenging free radicals and reducing oxidative stress. It also has anti-inflammatory properties that help mitigate chronic inflammation associated with metabolic disorders (Chen *et al.*, 2020). The antioxidant and anti-inflammatory effects of gallic acid contribute to better glycemic control and reduced risk of diabetes related complications. Its protective effects against oxidative damage support overall health and wellbeing (Li *et al.*, 2021).

2.8 Resveratrol

Resveratrol is a stilbenoid characterized by its structure of two phenol rings connected by a vinylene group. It is registered in various plants, including Mulberry. Resveratrol exerts its effects through its antioxidant and anti-inflammatory properties. It enhances insulin sensitivity, reduces oxidative stress, and modulates inflammatory pathways (Mahesh *et al.*, 2017). Resveratrol also has potential benefits for cardiovascular health. Resveratrol's ability to improve insulin sensitivity and reduce oxidative stress makes it a valuable compound for diabetes management. Its cardiovascular benefits further support its role in overall health maintenance (Zhang *et al.*, 2018).

2.9 Ellagic acid

Ellagic acid is a polyphenolic compound with a structure consisting of two phenolic rings connected by a central core. It is found in various fruits and vegetables, including Mulberry. Ellagic acid functions as an antioxidant, reducing oxidative stress and inflammation (Ma *et al.*, 2022). It also has potential antidiabetic effects by modulating glucose metabolism and improving insulin sensitivity. The antioxidant and anti-inflammatory properties of ellagic acid contribute to better glycemic control and reduced risk of diabetes related complications. Its comprehensive health benefits support overall metabolic health and wellbeing (Kim *et al.*, 2007).

3. Percentage composition of various chemical compounds found in Mulberry

The percentage composition of various chemical compounds commonly found in Mulberry plant and its natural products, indicating their nutritional and therapeutic potential. Flavonoids range from 1-2% and are known for their antioxidant and anti-inflammatory properties. Anthocyanins registered around in 0.05-2.0%, which contribute to the vibrant colors of plants and possess strong antioxidant capabilities. Phenolic acids (0.01-0.5%) are also effective antioxidants that help reduce inflammation and combat free radical damage. Alkaloids (0.1-0.5%) have potent medicinal properties, thus often serving as the basis for various pharmaceutical drugs. Triterpenoids (0.05-0.3%) are known for their anti-inflammatory and anticancer properties, while sterols (0.01-0.1%), particularly phytosterols, will help lower cholesterol levels. Vitamins present in small amounts (0.02%) were crucial for various bodily functions. Fatty acids recorded at 1% will provide essential nutrients, including omega-3s and omega-6s, which are vital for heart health. Polysaccharide levels were found to be 1-5%, valued for their immunomodulatory and energy providing benefits. Carotenoids (0.01-0.05%) function as antioxidants and are precursors to vitamin A. Lastly, amino acids (1-2%) are essential for protein synthesis, thereby supporting muscle repair and overall health. This diverse composition of various chemical compounds and their levels present underlines the therapeutic versatility of Mulberry plants.

4. Health benefits of Mulberry

4.1 Diabetes management

Mulberry leaves and fruits have shown efficacy in lowering blood glucose levels due to the presence of DNJ, which inhibits α -glucosidase activity. Clinical studies have confirmed its potential in managing type 2 diabetes (Ramesh *et al.*, 2024).

4.2 Cardiovascular health

Flavonoids and phenolic compounds in Mulberry have demonstrated cardiovascular protective effects (Verma *et al.*, 2022). These compounds help in reducing blood pressure, thus lowering cholesterol levels and preventing atherosclerosis (Shreelakshmi *et al.*, 2021).

4.3 Antioxidant and anti-inflammatory effects

The antioxidant properties of Mulberry are thus attributed to flavonoids and phenolic acids, which help mitigate oxidative stress and inflammation, thus contributing to the prevention of chronic diseases such as cancer and neurodegenerative disorders (Saeed *et al.*, 2023).

4.4 Immune system support

More vitamin C content in Mulberry fruits facilitates immune function (Priya *et al.*, 2023). Additionally, the anti-inflammatory properties support overall immune health (Venkatesh *et al.*, 2008).

5. Comparative analysis with other medicinal combinations

5.1 Mulberry vs. Ginseng

Ginseng (*Panax ginseng*) is renowned for its adaptogenic and antifatigue properties. When compared to Mulberry, ginseng offers similar benefits in terms of immune support and stress reduction, but Mulberry's additional benefits in glycemic control and cardiovascular health provide a broader therapeutic profile (Gundogdu *et al.*, 2018).

5.2 Mulberry vs. Garlic

Garlic (*Allium sativum*) is widely used for cardiovascular health due to its allicin content. While garlic is effective in lowering cholesterol and blood pressure, Mulberry's combination of flavonoids and phenolic acids offers a multifaceted approach to cardiovascular health and glycemic control (Yuan and Zhao, 2017).

5.3 Mulberry vs. Turmeric

Turmeric (*Curcuma longa*) is known for its potent anti-inflammatory and antioxidant properties due to curcumin. Mulberry complements these effects with its own antioxidant profile and additional benefits for diabetes management, thereby making a combination of Mulberry and turmeric a powerful therapeutic approach (Maqsood *et al.*, 2022).

5.4 Mulberry vs. Green tea

Green tea (*Camellia sinensis*) is celebrated for its catechins, which provide antioxidant and anti-inflammatory benefits. Mulberry's diverse range of bioactive compounds, including flavonoids and alkaloids, offers complementary benefits, particularly in managing blood sugar levels (Marchetti *et al.*, 2022).

6. Applications

Mulberry extracts and supplements are increasingly available and utilized for their health benefits (Bharathi *et al.*, 2023). Future research should focus on optimizing extraction methods and standardizing dosages to enhance therapeutic efficacy. Incorporating Mulberry into functional foods can offer additional health benefits. Research into the synergistic effects of Mulberry with other functional ingredients can lead to innovative health products. Traditional medicine has long utilized Mulberry products to enhance digestive

health, boost immunity, and support cognitive function (Lee *et al.*, 2018). With its broad spectrum of therapeutic actions, Mulberry is increasingly being incorporated into modern nutraceuticals and functional foods aimed at preventing and treating chronic diseases (Priya, 2023). The continued exploration of Mulberry's bioactive compounds holds promise for the development of natural, plantbased remedies to improve human health and wellbeing (Sanchez *et al.*, 2015). Additional clinical trials are needed to confirm the therapeutic potential of Mulberry and its related products. Comparative studies with other medicinal herbs will provide a clearer understanding of its efficacy and safety profile (Teodoro *et al.*, 2019).

7. Future prospects

While the bioactive compounds in Mulberry show significant promise in addressing various human health problems, further research is needed to fully harness their therapeutic potential. Several areas of investigation remain unexplored (Afzal *et al.*, 2021). More clinical trials are required to validate the efficacy and safety of Mulberry derived compounds such as 1-deoxynojirimycin (DNJ) and polyphenols in treating chronic conditions like diabetes, cardiovascular diseases, and cancer. Although, *in vitro* and animal studies have shown positive results, translating these findings into human applications will require extensive controlled trials to assess optimal dosages, longterm effects, and potential side effects (Ma *et al.*, 2021). Furthermore, understanding the bioavailability and metabolism of Mulberry's bioactive compounds is crucial. Many plantderived compounds face challenges in absorption and stability in the human body (Ju *et al.*, 2018). Research into formulation technologies that enhance the bioavailability and efficacy of these compounds, such as nanoencapsulation or the use of synergistic ingredients, could lead to more effective therapeutic products. Moreover, exploring the genetic diversity of Mulberry species and their variations in bioactive compound content may reveal specific cultivars with superior health benefits (Kadam *et al.*, 2019). Studies on sustainable cultivation practices and optimizing extraction methods for these compounds could further expand their commercial applications in pharmaceuticals and nutraceuticals (Bilawal *et al.*, 2021). So, there is a need for longterm studies on the safety and potential interactions of Mulberry products with conventional medications. Given Mulberry's growing use in complementary medicine and understanding these interactions is vital to ensure individual safety. In the future, continued research will be key to unlocking the full therapeutic potential of Mulberry bioactive compounds in modern healthcare (Kishore and Kumar, 2020).

8. Conclusion

Mulberry (*Morus* spp.) and its bioactive compounds represent a valuable natural resource with significant potential to address various human health problems. Rich in diverse phytochemicals such as flavonoids, alkaloids, polyphenols, anthocyanins, and vitamins, Mulberry offers a range of therapeutic effects including antioxidant, anti-inflammatory, antidiabetic, antimicrobial, and anticancer properties. Among its most studied compounds is 1-deoxynojirimycin (DNJ), which shows great efficacy in managing type 2 diabetes by regulating postprandial blood glucose levels. Similarly, polyphenols and anthocyanins present in Mulberry contribute to cardiovascular health by reducing oxidative stress and inflammation, while their neuroprotective effects may help prevent neurodegenerative diseases like Alzheimer's and Parkinson's. Beyond diabetes and cardiovascular

diseases, Mulberry compounds play a role in regulating lipid metabolism, lowering cholesterol, and preventing obesity related complications. They also exhibit antimicrobial activity, thus making them effective against various infections while their anti-inflammatory properties aid in managing chronic conditions like arthritis and inflammatory bowel diseases. Moreover, traditional medicine has long recognized the benefits of Mulberry in enhancing digestive health, boosting immunity, and improving cognitive function. Despite the promising health benefits of Mulberry, further research is necessary to fully understand its therapeutic potential. More clinical trials, improved bioavailability studies, and longterm safety assessments are needed to translate the findings from laboratory and animal studies to effective human treatments. Continued exploration of Mulberry's bioactive compounds, along with advances in sustainable cultivation and extraction methods, holds immense potential for developing natural and plantbased therapies. In conclusion, Mulberry and its bioactive compounds have become valuable components of modern healthcare, thus offering natural alternatives for preventing and treating chronic diseases, thus enhancing overall human wellbeing.

Acknowledgements

We extend our sincere appreciation to the Department of Sericulture, Forest College and Research Institute, Tamil Nadu Agricultural University, Mettupalayam, for their invaluable assistance.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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Citation

H.B. Roghan, I. Sekar, B. Karthick Mani Bharathi, S. Susikaran, M. Tilak and B. Sivakumar (2024). Bioactive compounds in Mulberry (*Morus* spp.) and their products in curing human health problems: A comparative analysis. *Ann. Phytomed.*, **13(2):291-297. <http://dx.doi.org/10.54085/ap.2024.13.2.28>.**