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PHYTOCHEMICALS IN MULBERRY ROOT: COMPOSITION AND THERAPEUTIC APPLICATIONS

N. R. Kiran^{1*}, Vijay Settu², H. Gunashekhar³, B. Manjunath⁴, S. Manju Prem⁵, R. Karthik⁶, Harishkumar Jayaram⁷, Damodhara G N⁸ and Karthik R⁹

¹UDepartment of Plant Biotechnology, University of Agricultural Sciences, GKVK, Bengaluru - 560 065, India.

²CSB-Silkworm Seed Production Centers, National Silkworm Seed Organization, Dakshinbawanipur - 733 132, India.

³ICAR-National Dairy Research Institute, Southern Regional Station, Bangalore - 560 030, India.

⁴The Graduate School, ICAR-Indian Agriculture Research Institute, New Delhi - 110 012, India.

⁵College of Agriculture, Vellayani, Thiruvananthapuram - 695 522, (Kerala Agriculture University), India.

^{6,9}Chaudhary Sarwan Kumar Himachal Pradesh Krishi Vishvavidyalaya, Palampur - 176 062, India.

⁷CSB - Silkworm Seed Production Center, National Silkworm Seed Organization, Berhampore, India.

⁸Manasagangothri University, Musuru - 570 005, India

*Corresponding author e-mail : kirannr833@gmail.com

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ABSTRACT : Mulberry (family Moraceae) has been historically used in traditional and modern medicine. This review explores the bioactive compounds in mulberry roots, their chemical composition, biological activities, traditional uses and modern applications. Mulberry roots contain phytochemicals with significant therapeutic potential, including antioxidant, anti-inflammatory, antidiabetic and antitumor effects. Mulberry root extracts, rich in compounds like morusin, kuwanon C and sanggenons, exhibit potent anti-inflammatory properties by inhibiting inflammatory mediators and modulating immune responses. These extracts also possess strong antioxidative effects due to compounds such as morusin and oxyresveratrol, which neutralize reactive oxygen species and protect cells from oxidative stress. The antidiabetic properties are attributed to bioactive compounds that regulate blood glucose levels and enhance insulin sensitivity. Studies indicate that these extracts lower blood glucose, improve insulin production and protect pancreatic β cells. Additionally, mulberry root extracts demonstrate antitumor activities by inducing apoptosis and inhibiting cell proliferation in various cancer cell lines. Compounds like sanggenol M and mulberofurans have shown cytotoxic effects against leukemia, melanoma and colorectal cancer cells. The anti-dopaminergic effects of these extracts make them potential candidates for managing psychotic disorders, as they reduce aggression, enhance catalepsy and decrease stereotyped behavior in animal models. Recent research highlights the potential of mulberry root extracts in developing pharmaceuticals and nutraceuticals for metabolic health and chronic disease prevention. Future research should focus on clinical trials to validate their efficacy and safety in humans, bioavailability studies for optimizing therapeutic use, and mechanistic studies to elucidate molecular pathways. Standardization and quality control measures are essential for ensuring consistency and regulatory approval. In conclusion, mulberry roots are a valuable source of bioactive phytochemicals with diverse health benefits. Integrating traditional knowledge with contemporary scientific research can enhance the therapeutic applications of mulberry roots in modern medicine.

Key words : Mulberry, root extract, anti-inflammatory, antioxidant, anti-dopamine.

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INTRODUCTION

Mulberry belongs to the genera *Morus* and is classified under the family moraceae. Mulberry is considered to be originated in the border area of the Indo-Chinese region. This genus is broadly distributed in Asia, Africa, Europe, South and North America and broadly observed in the Himalayas. Three different types of

mulberries are mainly known due to its natural colour as black, white, and red mulberry locally called as shahtut, chinni, and tut in Northern India. Mulberry is a fast-growing deciduous plant, and it can grow under variable climatic conditions from tropical to temperate. Mulberry (*Morus* spp.) is a plant with a rich history of use in both traditional and modern medicine. While, the leaves and

Table 1 : Chemical compounds identified by in the mulberry roots were listed according to the class with reference.

S. no.	Group	Compounds	References
1	2-arylbenzofurans	2-(1,3,3-trimethyl-7-oxabicyclo[2.2.1]hept-2-ylmethyl-3-methoxy-5,6-dihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		2-(6,7-dihydroxy-3,7-dimethyl-2-octen-1-yl)-3,5,6-trihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		2-(6,7-dihydroxy-3,7-dimethyl-2-octen-1-yl)-3-methoxy-5,6-dihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		2-(6-hydroxy-3,7-dimethyl-2,7-octadien-1-yl)-3-methoxy-5,6-dihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		2-[[3-methyl-3-(4-methyl-3-penten-1-yl)-2-oxiranyl]methyl]-3',5,6-trihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		4-(6,6-dimethyl-5-hydroxyl-2-methylenecyclohexylmethyl)-3,5,6-trihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		4'-(6,7-dihydroxy-3,7-dimethyl-2-octen-1-yl)-3,5,6-trihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		4-(6-hydroxy-3,7-dimethyl-2,7-octadien-1-yl)-3,5,6-trihydroxy-2-arylbenzofuran	Wei <i>et al</i> (2016)
		Albafuran A, B	Wei <i>et al</i> (2016)
		Artoindonesianin O	Wei <i>et al</i> (2016)
		Moracin C,D,E,I,M,N,O,P,Q,R	Wei <i>et al</i> (2016)
		Mornigrol D	Wei <i>et al</i> (2016)
		Mulberrofuran A,D,L,W,Y	Wei <i>et al</i> (2016)
		Mulberroside C	Wei <i>et al</i> (2016)
2	Alkaloids	1-deoxynojirimycin	Kiran <i>et al</i> (2019)
		N-methyl-1-deoxynojirimycin	Kimura <i>et al</i> (1995)
		(2R,3R,4R)-2-hydroxymethyl-3,4-dihydroxypyrrolidine-N-propionamid	Asano <i>et al</i> (2001)
		(2R,3R,4R)-2-hydroxymethyl-3,4-dihydroxypyrrolidine-N-propionamid	Asano <i>et al</i> (2001)
		(2R,3R,4R)-2-Hydroxymethyl-3,4-dihydroxypyrrolidine-N-propionamide	Asano <i>et al</i> (2001)
		1,4-dideoxy-1,4-imino-(2-O-, -D-glucopyranosyl)-D-arabinitol	Asano <i>et al</i> (2001)
		1,4-Dideoxy-1,4-imino-(2-O-β-D-glucopyranosyl)-D-arabinitol	Asano <i>et al</i> (2001)
		1,4-dideoxy-1,4-imino-D-arabinitol	Asano <i>et al</i> (2001)
		1,4-Dideoxy-1,4-imino-D-arabinitol	Asano <i>et al</i> (2001)
		1,4-dideoxy-1,4-imino-D-ribitol	Asano <i>et al</i> (2001)
		1,4-dideoxy-1,4-imino-D-ribitol	Asano <i>et al</i> (2001)
		1-Deoxynojirimycin	Asano <i>et al</i> (2001)
		2-O-R-D-galactopyranosyl-1-deoxynojirimycin	Yagi (1976)
		3-epi-fagomine	Asano <i>et al</i> (2001)
		3-O-, -D-glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (2001)
		3-O-β-D-Glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (2001)
		4-O-, -D-glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (2001), Asano <i>et al</i> (2001)
		4-O-, -D-glucopyranosyl-fagomine	Wei <i>et al</i> (2016)
		4-O-β-D-Glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (2001)
		4-O-β-D-Glucopyranosyl-fagomine	Wei <i>et al</i> (2016)

Table 1 continued...

Composition and therapeutic applications of phytochemicals in mulberry root

Table 1 continued...

		6-O-, -D-glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (1994), Asano <i>et al</i> (2001)
		6-O-, -D-glucopyranosyl-1-deoxynojirimycin	Wei <i>et al</i> (2016)
		6-O-β-D-Glucopyranosyl-1-deoxynojirimycin	Asano <i>et al</i> (2001)
		Albafuran C	Wei <i>et al</i> (2016)
		Calystegin B (1α,2β,3α,4β-tetrahydroxy-nor-tropane)	Asano <i>et al</i> (2001)
		CalystegineB1	Asano <i>et al</i> (1994), Asano <i>et al</i> (2001)
		CalystegineB2	Asano <i>et al</i> (19950), Asano <i>et al</i> (2001)
		Fagomine	Asano <i>et al</i> (2001)
3	Diels–Alder-type adducts	Albasin A;B	Ha <i>et al</i> (2018), Liu <i>et al</i> (2023)
		Australisine A;B;C	Wei <i>et al</i> (2016)
		Cathayanon A;B	Wei <i>et al</i> (2016)
		Chalcomoracin	Wei <i>et al</i> (2016)
		Kuwanon G(Moracenin B or Albanin F);H;L	Wei <i>et al</i> (2016), Guo <i>et al</i> , (2019), Lee <i>et al</i> (2024)
		Kuwanon J 2,4,10-tri methyl ether	Wei <i>et al</i> (2016)
		Mongolicin C;D	Wei <i>et al</i> (2016), Liu <i>et al</i> (2023)
		Morusalbonol A	Wei <i>et al</i> (2016)
		Mulberrofuran C;F,F,G,H,J,K;Q	Wei <i>et al</i> (2016), Liu <i>et al</i> (2023)
		Sanggenon O;B;D;E;G;M;T;C	Wei <i>et al</i> (2016), Liu <i>et al</i> (2023)
		Soroceal	Wei <i>et al</i> (2016)
		Soroceal B	Wei <i>et al</i> (2016)
		Leachianone G,	Ha <i>et al</i> (2018)
		Inethermulberrofuran C,	Ha <i>et al</i> (2018)
		Mongolicin A;C	Liu <i>et al</i> (2023)
		Morusalbin A;B;C;D	Ha <i>et al</i> (2018), Liu <i>et al</i> (2023)
		Sanggenon G; T; M	Liu <i>et al</i> (2023)
		Yunanensin A	Liu <i>et al</i> (2023)
		Albanol B	Liu <i>et al</i> (2023)
		Chalcomoracin A;B	Liu <i>et al</i> (2023)
Chalcomoracin B	Liu <i>et al</i> (2023)		
4	Stilbenes	Mulberrofuran B	Liu <i>et al</i> (2023)
		Sanggenofuran A	Liu <i>et al</i> (2023)
		Mulberrofuran H	Liu <i>et al</i> (2023), Ha <i>et al</i> (2018)
		(E)-4-Isopentenyl-3,5,2',4'-tetrahydroxystilbene (40)	Liu <i>et al</i> (2023)
		Moracin M	Liu <i>et al</i> (2023)

Table 1 continued...

Table 1 continued...

		Moracin S	Liu <i>et al</i> (2023)
		Moracin P	Liu <i>et al</i> (2023)
		Moracin O	Liu <i>et al</i> (2023)
		Morusalfuran A; B; C; D; F	Liu <i>et al</i> (2023)
		Morusibene A	Liu <i>et al</i> (2023)
		Mulberrofuran D2	Liu <i>et al</i> (2023)
		Oxyresveratrol-2-O- β -D-glucopyranoside	Gryn <i>et al</i> (2022)
		Oxyresveratrol-3-O- β -D-glucopyranoside	Gryn <i>et al</i> (2022)
		Oxyresveratrol-3-O- β -glucoside	Gryn <i>et al</i> (2022)
		Cis-mulberroside A	Qiu <i>et al</i> (1999)
		Mulberroside C	Qiu <i>et al</i> (1999)
		Oxyresveratrol-2,32 -O- α -D-diglycoside	Qiu <i>et al</i> (1999)
		Oxyresveratrol-2-O- α -D-glucuronide-32 -O-sulfate	Qiu <i>et al</i> (1999)
		Oxyresveratrol-32 -O- β -D-glucopyranoside	Qiu <i>et al</i> (1999)
		β -Sitosterol	Qiu <i>et al</i> (1999)
5	Flavonoid	2,4,2',4'-tetrahydroxychalcone	Wei <i>et al</i> (2016)
		2,4,5-trihydroxy-3-(777-hydroxydimethyl)propyl-2''-dimethylpyrano(5,6:6,7)-flavone	Wei <i>et al</i> (2016)
		3-geranyl-3-prenyl-2,4,5,7-tetrahydroxyflavone	Wei <i>et al</i> (2016)
		5,7,2'-trihydroxyflavanone-4-O- β -D-glucoside	Wei <i>et al</i> (2016)
		5-2'-dihydroxyflavanone-7, 4'-di-OD-glucose	Wei <i>et al</i> (2016)
		5-geranyl-4-methoxy-5,7,2-trihydroxyflavone	Wei <i>et al</i> (2016)
		5-geranyl-5,7,2,4-tetrahydroxyflavone	Wei <i>et al</i> (2016)
		7-methoxy-5,4'-dihydroxyflavanonol	Wei <i>et al</i> (2016)
		Cudraflavone B	Wei <i>et al</i> (2016)
		Cyclomorusin	Wei <i>et al</i> (2016), Deshpande <i>et al</i> (1968)
		Cyclomulberrin	Wei <i>et al</i> (2016), Deshpande <i>et al</i> (1968)
		Cyclomulberrochromene	Deshpande <i>et al</i> (1968)
		Hydroperoxide	Deshpande <i>et al</i> (1968)
		Kuwanon A;B;C;E;I;K;S;T;U;Y;Z	Wei <i>et al</i> (2016)
		Leachianone G	Wei <i>et al</i> (2016)
		Leachinone G	Deshpande <i>et al</i> (1968)
		Licoflavone C	Wei <i>et al</i> (2016)
		Moracenin A-D	Deshpande <i>et al</i> (1968)
		Morachalcone A	Wei <i>et al</i> (2016)
		Moralbanone	Deshpande <i>et al</i> (1968)
		Morusin	Wei <i>et al</i> (2016)
		Morusin 4-glucoside	Wei <i>et al</i> (2016)
		Mulberrin	Deshpande <i>et al</i> (1968)
		Mulberrochromene	Deshpande <i>et al</i> (1968)

Table 1 continued...

Table 1 continued...

		Mulberroside C	Deshpande <i>et al</i> (1968)
		Neocyclomorusin	Wei <i>et al</i> (2016)
		Norartocarpanone	Wei <i>et al</i> (2016)
		Norartocarpetin	Wei <i>et al</i> (2016)
		Oxydihydromorusin	Wei <i>et al</i> (2016)
		Oxydihydromorusin (morusinol)	Deshpande <i>et al</i> (1968)
		Prenylated Flavonoid (7, 2', 4', 6'-tetrahydroxy-6-geranylflavanone)	Hisayoshi <i>et al</i> (2004)
		Rudraflavone B	Deshpande <i>et al</i> (1968)
		Sanggenol A;L;N;Q;A;B;C;D;E;F;H;L;M;N;O;P;C;D	Wei <i>et al</i> (2016), Deshpande <i>et al</i> (1968)
		Steppogenin-4-O- β -D-glucoside	Wei <i>et al</i> (2016)
		Steppogenin-7,4'-di-O- β -D-glucoside	Wei <i>et al</i> (2016)
		Steppogenin-7-O- β -D-glucoside	Wei <i>et al</i> (2016)
		β -Acetyl-amyrin	Deshpande <i>et al</i> (1968)
6	Terpinoids	uvoval	Yang <i>et al</i> (2010)
		α -amyrin acetate	
		5,7,22 -trihydroxyflavanone-42 -O- β -d-glucoside	
		Betulinic acid	Yang <i>et al</i> (2011)
		Ursolic acid	Yang <i>et al</i> (2011)
7	Stilbenoids	Alabafuran A	Yang <i>et al</i> (2011)
		Artoindonesianin O	Yang <i>et al</i> (2011)
		32, 52 -Dihydroxy-6-methoxy-7-prenyl-2-arylbenzofuran	Yang <i>et al</i> (2011)
		Moracins C, D, M-P, R, V-Y	Yang <i>et al</i> (2011)
		Mulberrofurans L, Y	Yang <i>et al</i> (2011)
		Mulberrosides A, B	Yang <i>et al</i> (2011)
		Oxyresveratrol	Qiu <i>et al</i> (1998)
8	Coumarins	5, 7-Dihydroxycoumarin 7-O- β -d-apiofuranosyl-(1 \rightarrow 6)-O- β -D-glucopyranoside	Yang <i>et al</i> (2011)
		5, 7-Dihydroxycoumarin 7-O- β -D-glucopyranoside	Yang <i>et al</i> (2011)
9	Glycoside	2 methylene 3 methoxy 2, 5 dihydrofuron 4- o- β D-Glucopyranoside	Wei <i>et al</i> (2016)

fruits of the mulberry are well-known for their health benefits, the roots contain a diverse array of phytochemicals that offer significant therapeutic potential. This article will provide a detailed exploration of the phytochemicals present in mulberry roots, examining their chemical composition, biological activities, traditional uses, modern applications and future research directions. The goal is to highlight the importance of mulberry roots in health and medicine, supported by both historical knowledge and contemporary scientific research.

Bio-active compounds present in the mulberry root

The root bark of mulberry tree (*Morus* species, Moraceae) has been used by human beings for at least 4000 years (Yin *et al*, 2017). The earliest written

reference to the use of mulberry tree is contained in the first Chinese dispensatory “Shen Nong Ben Cao Jing” whose original anonymous volume probably appeared by the end of the third century. In the book, the root bark of the plant is called as ‘Sang Bai Pi’. It has been demonstrated that both mulberry plant nutraceuticals and phytochemicals have biological attributes that include antioxidant, anti-stress, anti-obesity, antidepressant, anxiolytic, anti-diabetic, anticancer, antimicrobial, anti-inflammatory, cytotoxic, neuroprotective, anti-aging, hepatoprotective, cardio-vascular and anti-atherosclerotic activity.

Pharmacological effects of mulberry root extract

Anti-inflammatory

Anti-inflammatory effects involve the reduction of inflammation, a normal immune response characterized by increased blood flow, swelling and pain. Anti-inflammatory agents work by inhibiting inflammatory mediators, modulating immune responses and targeting specific inflammatory pathways. They include steroidal and non-steroidal drugs, as well as natural compounds found in plants. These agents provide pain relief, promote tissue repair, and may prevent chronic diseases associated with inflammation, though individual responses and potential side effects should be considered. Mulberry root extracts demonstrate potent anti-inflammatory properties through various mechanisms, making them promising candidates for therapeutic intervention in inflammatory conditions.

Mulberry root extracts inhibit arachidonate metabolism and cyclooxygenase (COX) activity, as evidenced by the suppression of prostaglandin synthesis. Compounds such as morusin, kuwanon C and sanggenons exhibit inhibitory effects on COX activity, reducing the production of inflammatory prostaglandins (Rollinger *et al*, 2005). Additionally, mulberry root extracts suppress the production of inflammatory mediators like nitric oxide (NO), prostaglandin E2 (PGE2) and cytokines such as TNF- α and IL-6 (Wu *et al*, 2020). This suppression occurs through the inhibition of NF- κ B activation, a key regulator of inflammatory responses. Numerous bioactive compounds found in mulberry root extracts contribute to its anti-inflammatory effects. Compounds like oxyresveratrol, cudraflavone B, caffeic acid and p-coumaric acid modulate inflammatory pathways by inhibiting NF- κ B activation or cytokine production. Moreover, mulberry root extracts exhibit anti-allergenic activities by inhibiting mast cell activation, histamine release and Th2 cytokine production, suggesting their potential in allergic conditions (Chai *et al*, 2005). Furthermore, ethanol and water extracts of mulberry roots alleviate symptoms of airway inflammation and bronchitis-like conditions. Compounds like moracin M also show promise as phosphodiesterase-4 inhibitors, indicating their potential in inflammatory respiratory diseases (Wei *et al*, 2016). In conclusion, Mulberry root extracts exert anti-inflammatory effects through inhibition of inflammatory mediators, modulation of NF- κ B signaling and suppression of allergic responses. These findings suggest the therapeutic potential of mulberry root extracts in various inflammatory conditions.

Antioxidative effects

Antioxidative effects refer to the ability of a substance to neutralize or counteract the harmful effects of reactive oxygen species (ROS) and free radicals in the body. ROS, including molecules like superoxide radicals, hydroxyl radicals and hydrogen peroxide are produced naturally during metabolic processes, but can also be generated due to external factors like pollution, radiation, and unhealthy lifestyle habits. Antioxidants work by donating electrons to unstable ROS, thereby preventing them from damaging cells, DNA, proteins and lipids through oxidative stress. Oxidative stress is implicated in various diseases and aging processes. Antioxidants help maintain the balance between ROS production and the body's ability to detoxify them, thus protecting cells from damage. Numerous studies have highlighted the importance of antioxidants in health and disease prevention. They play a role in reducing inflammation, preventing chronic diseases such as cardiovascular diseases, cancer and neurodegenerative disorders and promoting overall well-being. The antioxidative effects of mulberry root extracts are attributed to a diverse array of bioactive compounds present in the extract. Studies have consistently shown that mulberry root extracts possess potent antioxidant properties, making them valuable in combating oxidative stress-related disorders. Mulberry root extract demonstrates strong free radical scavenging activity, which helps neutralize reactive oxygen species (ROS) responsible for oxidative damage in the body. Additionally, its ability to inhibit xanthine oxidase and lipid peroxidation further contributes to its antioxidative effects, protecting cells and tissues from oxidative damage (Wei *et al*, 2016).

Several specific compounds within mulberry root extracts have been identified for their antioxidative activities. Morusin, Australone B, moracins, chalcomoracin, oxyresveratrol and others exhibit scavenging effects against various ROS, preventing oxidative damage (Panek-Krzy eko). Mulberroside A stands out for its liver protective action, guarding against hepatotoxicity induced by substances like CCl₄ (Shi *et al*, 2023). Moreover, mulberry root extracts contain compounds like albanol B, 2-methylene-3-methoxy-2,5-dihydrofuran-4-O- β -D-glucopyranoside and mulberrofuran G, which show promising antioxidant activities in assays such as DPPH and ABTS, indicating their potential for reducing oxidative stress. The presence of phenolic compounds, including flavonoids, stilbenes and Diels–Alder-type adducts, further contributes to the antioxidant capacity of Mulberry root extracts. These compounds are known for their ability to scavenge free

radicals and protect against oxidative damage (Wei *et al.*, 2016). Overall, the antioxidative effects of mulberry root extracts are significant and versatile, offering protection against oxidative stress-related conditions such as inflammation, aging and various diseases. Utilizing mulberry root extracts as natural antioxidants could provide promising therapeutic avenues for managing oxidative stress and promoting overall health and well-being.

Anti-diabetic effect

The basis of antidiabetic effects involves substances that help regulate blood glucose levels and improve insulin sensitivity, making them crucial in managing diabetes (American Diabetes Association, 2022). Antidiabetic agents work through various mechanisms such as enhancing insulin production, promoting glucose uptake by cells, inhibiting glucose absorption in the gut and reducing insulin resistance (DeFronzo *et al.*, 2015). Additionally, they may also protect pancreatic β cells from damage and alleviate complications associated with diabetes, such as lipid peroxidation and oxidative stress. Natural compounds found in plant extracts often exhibit antidiabetic properties by targeting these mechanisms. These compounds include flavonoids, polyphenols, alkaloids and others, which can modulate glucose metabolism pathways and improve insulin signalling (Ríos and Francini, 2016). By targeting multiple pathways involved in diabetes, these agents offer comprehensive therapeutic effects.

Mulberry root extracts exhibit significant antidiabetic effects, with studies showing that both aqueous and ethanolic extracts lower blood glucose levels and improve insulin production in diabetic animals. These extracts also protect pancreatic β cells from degeneration, reduce lipid peroxidation and inhibit LDL atherogenic modification. The antidiabetic properties are attributed to various bioactive compounds present in mulberry roots, including Moran A, Moran 20 K, Morusin, Cyclomorusin, Neocyclomorusin, Kuwanon E, Moracin M, Betulinic acid, Steppogenin-4-O- β -D-glucoside, Mulberroside A, Ethyl β -resorcyate (ethyl 2,4-dihydroxybenzoate), 5,7-Dihydroxychromone and others. These compounds contribute to regulating glucose metabolism, enhancing insulin sensitivity and promoting glucose uptake by cells. Additionally, inhibitors targeting protein tyrosine phosphatase 1B (PTP1B) and α -glucosidase found in mulberry roots further aid in lowering blood glucose levels (Paudel *et al.*, 2018). Furthermore, mulberry root extracts exert lipid-lowering effects and have been reported to possess anti-hypertensive properties in animal studies (James *et al.*, 2024). Overall, these findings suggest the

potential of mulberry root extracts as therapeutic agents for managing diabetes and its complications (Wei *et al.*, 2016).

Antitumor effects

Antitumor effects of mulberry root extracts have been demonstrated through various mechanisms. Studies have shown that mulberry root extract exhibits cytotoxic activity against human leukemia cells, mouse melanoma cells and human colorectal cancer cells by inhibiting microtubule assembly, inducing cell growth arrest and apoptosis. Additionally, mulberry root extracts may be effective against multidrug-resistant cancer cells.

Several compounds isolated from mulberry roots have shown cytotoxic activities against various cancer cell lines. These compounds include sanggenol M, sanggenon C, australisines, mulberrofurans, moracin C, morusin, cyclomorusin and oxyresveratrol. Various mechanisms have been identified for their antitumor effects, such as inhibition of ornithine decarboxylase induction, antagonism for specific receptors, inhibition of protein kinase C and inhibition of hypoxia-inducible factor-1 accumulation (Yoshizawa *et al.*, 1989; Mihara *et al.*, 1995; Hu *et al.*, 1996; Dat *et al.*, 2009). Moreover, compounds like cudraflavone B, kuwanon E and 4'-O-methylkuwanon E exert antiproliferative and anti-inflammatory activities, suggesting their potential in cancer treatment (Kollar *et al.*, 2013).

Various other pharmacological effects

Mulberry root extracts exhibit various pharmacological effects attributed to their bioactive compounds. Cyclomorusin, morusin and kuwanon C have been shown to have anti-platelet effects, while morusin has also demonstrated anti-nociceptive effects. Mulberroside A exhibits liver protective and P-Glycoprotein inhibitory effects and compounds like sanggenons C, D, G and morusin are positive modulators of GABAA receptors. Additionally, various compounds including kuwanons, morusin, oxyresveratrol and cyclomorusin exhibit cholinesterase inhibitory effects. Sanggenol Q, kuwanon T and others have hepatoprotective effects, while compounds like moracins, oxyresveratrol and kuwanons have neuroprotective effects. Moreover, several compounds from Mulberry root extracts have shown tyrosinase inhibitory activities.

Stress management

The ethyl acetate soluble fraction of *Morus alba* showed significant potential in managing chronic restraint stress (RS)-induced disruptions in behavioral, biochemical and brain oxidative stress parameters. In this study, stress was induced in animals by confining them in an adjustable

cylindrical plastic tube for 3 hours daily over ten consecutive days. The anti-stress effects of the ethyl acetate soluble fraction of *M. alba* were evaluated by administering different doses (25, 50, 100 mg/kg) of the extract, with results compared to diazepam (1 mg/kg). The anti-stress efficacy was assessed through various behavioral and biochemical measures, including open field tests, cognitive function, leukocyte count, blood glucose and corticosterone levels. On the tenth day, the rats were sacrificed and biochemical assessments of lipid peroxidation, superoxide dismutase (SOD), catalase (CAT) and glutathione reductase (GSH) were conducted on the entire brain. The results indicated that *M. alba* treatment significantly reduced cognitive dysfunction, abnormal leukocyte counts, elevated glucose and corticosterone levels and improved SOD activity, lipid peroxidation, CAT and GSH levels. These findings suggest that *M. alba* has strong potential to alleviate stress-induced disorders (Nade *et al*, 2010).

Anti-dopamine effects

The methanolic extract of *M. alba* L. has been evaluated for its effects on dopaminergic function. In mice, the extract was tested on foot shock-induced aggression, metoclopramide- and haloperidol-induced catalepsy, amphetamine-induced stereotyped behavior, and phenobarbitone-induced sleep. The extract was administered at doses of 50, 100 and 200 mg/kg intraperitoneally, 30 minutes before testing (Yadav and Nade, 2008).

Results showed that the extract significantly enhanced haloperidol- and metoclopramide-induced catalepsy, reduced fights and increased latency to fight in foot shock-induced aggression, decreased amphetamine-induced stereotyped behaviour and extended phenobarbitone-induced sleep duration. These findings indicate that the methanolic extract of *M. alba* L. has strong anti-dopaminergic potential and may be useful as an alternative medicine for managing psychotic disorders (Nade *et al*, 2009).

Applications of mulberry root extracts in recent years

Recent studies have highlighted the potential of mulberry root extracts in the development of pharmaceuticals and nutraceuticals. Their antioxidant, anti-inflammatory and antidiabetic properties make them suitable for formulating supplements and herbal remedies aimed at improving metabolic health and preventing chronic diseases. Mulberry root extracts are being explored for their potential in developing drugs for diabetes, cancer and inflammatory diseases. The bioactive

compounds in mulberry roots offer multiple therapeutic targets, making them valuable in pharmaceutical research (Eo *et al*, 2014). The health-promoting properties of mulberry root phytochemicals have led to their inclusion in dietary supplements and functional foods. These products aim to enhance overall health, prevent disease, and promote longevity.

Future prospects

While significant progress has been made in understanding the phytochemical composition and biological activities of mulberry roots, further research is needed to fully elucidate their mechanisms of action and therapeutic potential.

Key areas for future research include:

- 1. Clinical Trials:** Rigorous clinical trials are needed to validate the efficacy and safety of mulberry root extracts in humans. These trials will help in translating preclinical findings into practical health applications.
- 2. Bioavailability Studies:** Understanding the bioavailability and metabolism of mulberry root phytochemicals is crucial for optimizing their therapeutic use. Studies on absorption, distribution, metabolism, and excretion will provide insights into how these compounds exert their effects in the body.
- 3. Mechanistic Studies:** Detailed mechanistic studies are required to elucidate the molecular pathways through which mulberry root phytochemicals exert their biological activities. These studies will help in identifying specific targets for therapeutic intervention.
- 4. Standardization and Quality Control:** Developing standardized extraction methods and quality control measures is essential for ensuring the consistency and efficacy of mulberry root-based products. Standardization will also facilitate the regulatory approval of these products.

CONCLUSION

Mulberry roots are a rich source of bioactive phytochemicals with diverse health benefits. The antioxidant, anti-inflammatory, antimicrobial, anticancer and antidiabetic properties of these compounds highlight the therapeutic potential of mulberry roots. As research continues to uncover their mechanisms and efficacy, mulberry roots may become an integral part of modern medicinal and nutraceutical formulations. This chapter has provided a comprehensive overview of the phytochemicals in mulberry roots and their health benefits, emphasizing the importance of integrating traditional knowledge with contemporary scientific research for the advancement of health and medicine.

REFERENCES

- Ahn Eunyeong, Jimin Lee, Young-Hee Jeon, Sang-Won Choi and Eunjung Kim (2017) Anti-diabetic effects of mulberry (*Morus alba* L.) branches and oxyresveratrol in streptozotocin-induced diabetic mice. *Food Sci. Biotechnol.* **26**, 1693-1702. <https://doi.org/10.1007/s10068-017-0223-y>
- Asano N, Kizu H, Oseki K, Tomioka E, Matsui K, Okamoto M and Baba M (1995) N-alkylated nitrogen-in-the-ring sugars: Conformational basis of inhibition of glycosidases and HIV-1 replication. *J. Medicinal Chem.* **38** (13), 2349-2356. <https://doi.org/10.1021/jm00013a012>
- Asano N, Nash R J, Molyneux R J and Fleet G W (2000) Sugar-mimic glycosidase inhibitors: Natural occurrence, biological activity and prospects for therapeutic application. *Tetrahedron: Asymmetry* **11**(8), 1645-1680. [https://doi.org/10.1016/S0957-4166\(00\)00113-0](https://doi.org/10.1016/S0957-4166(00)00113-0)
- Asano N, Oseki K, Kizu H and Matsui K (1994) Nitrogen-in-the-ring pyranoses and furanoses: Structural basis of inhibition of mammalian glycosidases. *J. Medicinal Chem.* **37**(22), 3701-3706. <https://doi.org/10.1021/jm00048a006>
- Asano N, Oseki K, Tomioka E, Kizu H and Matsui K (1994) N-containing sugars from *Morus alba* and their glycosidase inhibitory activities. *Carbohydrate Res.* **259** (2), 243-255. [https://doi.org/10.1016/0008-6215\(94\)84060-1](https://doi.org/10.1016/0008-6215(94)84060-1)
- Asano N, Yamashita T, Yasuda K, Ikeda K, Kizu H, Kameda Y and Ryu K S (2001) Polyhydroxylated alkaloids isolated from mulberry trees (*Morus alba* L.) and silkworms (*Bombyx mori* L.). *J. Agricult. Food Chem.* **49** (9), 4208-4213. doi.org/10.1021/jf010567e.
- Chai O H, Lee M S, Han E H, Kim H T and Song C H (2005) Inhibitory effects of *Morus alba* on compound 48/80-induced anaphylactic reactions and anti-chicken gamma globulin IgE-mediated mast cell activation. *Biol. Pharmaceut. Bull.* **28**(10), 1852-1858. <https://doi.org/10.1248/bpb.28.1852>
- Defronzo R A, Ferrannini E, Groop L, Henry R R, Herman W H, Holst J J and Raz I (2015) Type 2 diabetes mellitus. *Nat. Rev. Dis. Primers* **1**(1). <https://doi.org/10.1038/nrdp.2015.19>
- Deshpande V H, Parthasarathy P C and Venkataramn K (1968) Four analogues of artocarpin and cyclotocarpin from *Morus alba*. *Tetrahedron Letters* **9**(14), 1715-1719. [https://doi.org/10.1016/S0040-4039\(01\)99035-5](https://doi.org/10.1016/S0040-4039(01)99035-5)
- Eo H J, Park J H, Park, G H, Lee M H, Lee J R, Koo J S and Jeong J B (2014) Anti-inflammatory and anti-cancer activity of mulberry (*Morus alba* L.) root bark. *BMC Complement. Alter. Med.* **14**, 1-9. <https://doi.org/10.1186/1472-6882-14-200>
- Gryn-Rynko A, Sperkowska B and Majewski M S (2022) Screening and structure-activity relationship for selective and potent anti-melanogenesis agents derived from species of mulberry. *Molecules* **27**(24), 9011. <https://doi.org/10.3390/molecules27249011>
- Guo S, Liu L, Zhang S, Yang C, Yue W, Zhao H, Ho C T, Du J, Zhang H and Bai N (2019) Chemical characterization of the main bioactive polyphenols from the roots of *Morus australis* (mulberry). *Food and Function* **10**(10), 6915-6926. <https://doi.org/10.1039/C9FO01457H>
- Ha M T, Seong S H, Nguyen T D, Cho W K, Jeong Ah K, Ma J Y, Woo M H, Choi J S and Min B S (2018) Chalcone derivatives from the root bark of *Morus alba* L. act as inhibitors of PTP1B and α -glucosidase. *Phytochemistry* **155**, 114-125. <https://doi.org/10.1016/j.phytochem.2018.08.001>
- Hisayoshi K, Masashi Y and Koichi S (2004) A novel cytotoxic prenylated flavonoid from the root of *Morus alba*. *J. Insect Biotechnol. Sericol.* **73**(3), 113-116. <https://doi.org/10.11416/jibs.73.113>
- James A, Wang K, Chen Y and Wang Y (2024) Functional benefits of mulberry leaf tea or extracts to alleviate metabolic diseases: Current opinion and perspectives. *Food Bioscience* **59**, 104218. <https://doi.org/10.1016/j.fbio.2024.104218>
- Kiran T, Yuan Y Z, Andrei M, Fang Z, Jian G Z and Zhao J W (2019) 1-Deoxynojirimycin, its potential for management of non-communicable metabolic disorders. *Trends Food Sci. Technol.* **89**, 88-99. <https://doi.org/10.1016/j.tifs.2019.05.010>
- Lee J H, Kim H W, Kim SA, Ju W T, Kim S Y and Kim S J (2013) Hypoglycemic effect of *Morus alba* L. (white mulberry) leaves in streptozotocin-induced diabetic rats. *Europ. J. Integ. Med.* **5**(2), 71-76.
- Liu, Chen-Hao, Fei Liu and Liang Xiong (2023) Medicinal parts of mulberry (leaf, twig, root bark and fruit) and compounds thereof are excellent traditional chinese medicines and foods for diabetes mellitus. *J. Functional Foods* **106**, 105619. <https://doi.org/10.1016/j.jff.2023.105619>
- Nade V S and Yadav A V (2010) Anti-stress effect of ethyl acetate soluble fraction of *Morus alba* in chronic restraint stress. *Pharmaceutical Biology* **48**(9), 1038-1046. <https://doi.org/10.3109/13880200903473741>
- Nade V S, Kawale L A, Naik R A and Yadav A V (2009) Adaptogenic effect of *Morus alba* on chronic footshock-induced stress in rats. *Indian J. Pharmacol.* **41**(6), 246-251. DOI: 10.4103/0253-7613.59921
- Panek-Krzyćko A and Stompor-Gorłacy M (2021) The pro-health benefits of morusin administration—An update review. *Nutrients* **13**, 3043. <https://doi.org/10.3390/nu13093043>
- Paudel P, Yu T, Seong S H, Kuk E B, Jung H A and Choi J S (2018) Protein tyrosine phosphatase 1B inhibition and glucose uptake potentials of mulberrofuran G, albanol B and kuwanon G from root bark of *Morus alba* L. in insulin-resistant HepG2 cells: An *in vitro* and *in silico* study. *Int. J. Mole. Sci.* **19**(5), 1542. <https://doi.org/10.3390/ijms19051542>
- Qiu F, He T Z and Zhang Y Q (2016) The isolation and the characterization of two polysaccharides from the branch bark of mulberry (*Morus alba* L.). *Arch. Pharmacol Res.* **39**, 887-896. <https://doi.org/10.1007/s12272-016-0742-8>
- Qiu F, Kano Y and Yao X (1999) Elucidation of the bioactive constituents in traditional Chinese medicine “Mori Cortex”. *Studies in Plant Science* **6**, 281-289. [https://doi.org/10.1016/S0928-3420\(99\)80035-4](https://doi.org/10.1016/S0928-3420(99)80035-4)
- Rollinger J M, Spitaler R, Menz M, Marschall K, Zelger R, Ellmerer E P and Stuppner H (2006) Venturia inaequalis-inhibiting diels-alder adducts from *Morus* root bark. *J. Agricult. Food Chem.* **54**(22), 8432-8436. <https://doi.org/10.1021/jf061871g>
- Shi B, Qian J, Miao H, Zhang S, Hu Y, Liu P and Xu L (2023) Mulberroside A ameliorates CCl₄ induced liver fibrosis in mice via inhibiting pro inflammatory response. *Food Sci. Nutr.* **11**(6), 3433-3441. <https://doi.org/10.1002/fsn3.3333>
- Wei, H., Zhu J J, Liu X Q, Feng W H, Wang Z M and Yan L H (2016) Review of bioactive compounds from root barks of *Morus* plants (Sang-Bai-Pi) and their pharmacological effects. *Cogent Chemistry* **2**(1). <https://doi.org/10.1080/23312009.2016.1212320>
- Wu Y X, Kim Y J, Kwon T H, Tan C P, Son K H and Kim T (2020) Anti-inflammatory effects of mulberry (*Morus alba* L.) root bark and its active compounds. *Nat. Product Res.* **34**(12), 1786-1790. <https://doi.org/10.1080/14786419.2018.1527832>
- Yadav A V and Nade V S (2008) Anti-dopaminergic effect of the

- methanolic extract of *Morus alba* L. leaves. *Indian J. Pharmacol.* **40**(5), 221-226. DOI: 10.4103/0253-7613.44154
- Yagi M, Kouno T, Aoyagi Y and Murai H (1976) The structure of moranoline, a piperidine alkaloid from *Morus* species. *J Agric Chem Soc Jpn.* **50**(11), 571–572. https://doi.org/10.1271/nogeikagaku1924.50.11_571 .
- Yang H, Chen H, Ma H and Xiao W (2010) Hypoglycemic activity of polysaccharide from root bark of *Morus alba* L. *J. Ethnopharmacol.* **129**(3), 349-352.
- Yin X L, Liu H Y and Zhang Y Q (2017) Mulberry branch bark powder significantly improves hyperglycemia and regulates insulin secretion in type II diabetic mice. *Food Nutr. Res.* **61**(1). <https://doi.org/10.1080/16546628.2017.1368847>
- Zhou Jin, Shun-xiang Li, Wei Wang, Xiao-yi Guo, Xiang-yang Lu, Xin-pei Yan, Dan Huang, Bao-yang Wei and Liang Cao (2013) Variations in the levels of mulberroside A, oxyresveratrol and resveratrol in mulberries in different seasons and during growth. *The Scientific World J.* **2013**, 380692. <https://doi.org/10.1155/2013/380692>