

An overview on clinical studies of *Morus* species with bioactivities of compounds providing supporting evidence

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ABSTRACT

Morus of the family Moraceae is a small plant genus having 19 species worldwide. Among the *Morus* species, *M. alba* (MA), *M. indica*, *M. nigra*, and *M. rubra* are economically important. Of these species, the medicinal values of the whole plant, leaf, fruit, twig, and root of MA are the most well-known. Most noteworthy are the anti-diabetic properties of MA. In this review, 23 clinical studies on anti-diabetic properties (5 in Japan) and 9 clinical studies on other pharmacological properties (4 in Thailand) of *Morus* species are described. The latter includes hypolipidemic, cognitive enhancement, coronary heart disease attenuation, anti-obesity, and climacteric improvement. Further studies on the molecular mechanisms of mulberry compounds, and their safety, distribution, absorption, metabolism, and excretion are needed.

INTRODUCTION

Morus of the family Moraceae is a small plant genus having 19 species worldwide [1]. Economically important species are *Morus alba* (white mulberry), *Morus indica* (MI, Indian mulberry), *Morus nigra* (MN, black mulberry), and *Morus rubra* (red mulberry). China has 11 *Morus* species of which 5 are endemic and 1 is introduced [2].

Morus alba L., comprising *M. alba* var. *alba* and *M. alba* var. *multicaulis*, is a fast-growing monoecious and deciduous shrub or medium-sized tree without buttress [2–5]. Young plants produce multiple stems via coppicing. The bark is brownish-gray with vertical fissures, lenticels, and white or cream-colored latex. Leaves of *M. alba* (MA) are glossy green, alternately arranged, cordate at the base, and acuminate at the apex. Leaf margins are serrated, leaf petioles are long and slender, and leaf blades vary from unlobed to almost palmate. Fruits are drupes or sorosis that are white when young, turning reddish when mature, and black when ripe [2–5]. Leaves, twigs, and maturing fruits of MA are shown in Figure 1.

The whole plant, leaf, fruit, twig, and root of MA have medicinal values. Chemical constituents comprise steroids, tannins, phytosterols, glycosides, alkaloids, carbohydrates, proteins, and amino acids, as well as saponins, triterpenes, phenols, flavonoids, benzofurans, anthocyanins, polysaccharides, anthraquinones, and glycosides [5–7]. Pharmacological properties include antioxidant, antimicrobial, anti-inflammatory, anti-diabetic, hypolipidemic, anti-obesity, anti-atherosclerotic, neuroprotective, hepatoprotective, tyrosinase inhibitory, and cardioprotective [5–7]. The beneficial effects of MA leave against cardiometabolic risks have been reviewed [8]. The chemical constituents, medicinal properties, clinical trials, and patents of twigs of MA (*Ramulus Mori*) have recently been reviewed [9].

In this review, the clinical studies of *Morus* species (mostly MA) to date are briefly described. These studies are categorized as anti-diabetic properties (2007–2022) and other pharmacological properties (2001–2021) in chronological order. Relevant to the findings of these studies are mention of compounds, their classes, and bioactivities.

CLINICAL STUDIES

Anti-diabetic properties

There are 23 clinical studies on anti-diabetic properties of *Morus* species (Table 1). Five studies were undertaken in

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Japan; three studies each in the USA, Korea, China, and India; and two studies each in Iran and the UK. Single studies were conducted in Thailand and Poland. All studies were on MA except one study on MN. Plant parts of MA clinically tested were mostly leaves with fruits and twigs lesser studied.

OTHER PHARMACOLOGICAL PROPERTIES

There are nine clinical studies on other pharmacological properties of *Morus* species (Table 2). Four



Figure 1. Leaves (left), twigs (middle), and maturing fruits (right) of *Morus alba*.

studies were undertaken in Thailand, two studies in China, and single studies were conducted in Japan, India, and Brazil. One study was tested on MN and MI each. Clinical studies on other pharmacological properties of *Morus* species include hypolipidemic (3), cognitive enhancement (2), coronary heart disease (CHD) attenuation (2), anti-obesity (1), and climacteric improvement (1).

BIOACTIVE COMPOUNDS

Anti-diabetic

Compounds in MA leaves, fruits, and twigs with anti-diabetic activities include 1-deoxynojirimycin (DNJ), quercetin, dihydroquercetin kaempferol, rutin, chlorogenic acid chalcone, morachalcone, and isobavachalcone [6,42,43]. Steppogenin-4'-*O*- β -D-glucoside and mulberroside A from the root bark of MA significantly reduced the fasting blood glucose level in alloxan-induced diabetic mice [44]. Rutin and quercetin-3-*O*- β -D-glucoside, two anti-diabetic flavonoids from the fruit of MA, improved glucose uptake in 3T3-L1

Table 1. Clinical studies on anti-diabetic properties of *Morus* species.

Description of clinical study	Reference
At Tohoku University, Sendai, Japan, an MA leaf powder rich in DNJ (1.5%) was clinically tested to determine the optimal dose to suppress PPG. Results showed that a dose of 0.8 and 1.2 g of the leaf powder significantly reduced PPG and secretion of insulin after 30–180 minutes.	[10]
In Minneapolis Medical Center, USA, the hypoglycemic effects of MLE were tested on healthy and T2D subjects. Changes in the blood glucose of subjects were monitored after ingesting 75 g sucrose in 500 ml of water with 1.0 g of MLE or placebo. Results showed that after 2 hours there was a significant difference in the blood glucose level between MLE and placebo for the control and diabetic groups. The decrease in glucose for MLE and placebo was 15 and 22 mg/dl for the control group, and 42 and 56 mg/dl for the T2D group.	[11]
The suppressive ability of confections containing MLE on PPG and PPI in healthy subjects was tested at Siebold University of Nagasaki, Japan. Healthy females participated in the clinical study. Daifuku, mochi, Mizu-yokan, and chiffon cake were ingested by each subject. The confections with a 10:1 ratio of MLE to sucrose were found to effectively suppress the PPG and PPI, by inhibiting the intestinal sucrase, suggesting its prebiotic effect.	[12]
At Nippon Medical School, Tokyo, Japan, the effect of DNJ-rich MLE on PPH was assessed in subjects having impaired glucose metabolism. Ingestion of MLE attenuated acute glycemia. After 12 weeks, the serum 1,5-AG in the extract group was significantly higher than in the placebo group.	[13]
Conducted at the Miharadai Hospital in Nagasaki, Japan, the study was attended by 10 patients with T2D and 10 healthy subjects. Results affirmed that PPG and PPI levels in T2D patients treated with sulfonylurea were significantly suppressed after ingestion of jelly containing 3.3 g of MLE.	[14]
At Ewha Woman's University, Seoul, Korea, a clinical study investigated the intake dosage of aqueous MLE (DNJ 3.6 mg/g) and the time necessary to reduce PPG levels after intake of 75 g maltose by 50 healthy subjects. Results showed that the ingestion of 2.5 or 5.0 g of MLE leaf extract at 30 and 60 minutes was necessary to suppress glucose levels in healthy subjects.	[15]
Research on the effect of mulberry tea in reducing PPG levels in T2D patients was conducted at Sri Jayadeva Institute of Cardiovascular Sciences and Research in Bangalore, India. A total of 20 diabetic patients consumed plain tea as control and 28 diabetic patients consumed mulberry tea as treatment. FBG was monitored after a standard breakfast. The PPG levels of all 48 patients were recorded 90 minutes after the consumption of 70 ml of tea with one teaspoon of sugar added. In the control and test groups, FBG levels were 179 and 154, and PPG values were 287 and 210, respectively. A highly significant reduction in the PPG level was observed in patients who consumed the mulberry tea compared with patients who consumed the plain tea.	[16]
Another clinical study conducted at the Department of Food Science and Technology, Seoul National University, Korea, showed that DNJ-enriched MLE improved PPG response in pre-diabetic subjects. With supplementation of 5 g/day of extract for 4 weeks, subjects exhibited significantly improved post-prandial glycemic control. The MLE has been standardized to contain 3.6 mg/g of DNJ.	[17]
The α -glucosidase inhibitory and post-prandial hypoglycemic effects of a standardized MLE were tested on 46 patients with IGT at Hallym University Hospital, Chuncheon, Korea. The randomized double-blind clinical trial investigated the α -glucosidase inhibition in patients with IGT. The inhibitory effects of rice coated with MLE (12 mg/100 g rice) were evaluated in a group of IGT patients and another group of normal persons towards PPG. Results showed that MLE had significant inhibition towards PPH in both groups.	[18]
The efficacy and safety of MA twig alkaloids for the treatment of T2D were assessed by the clinical study undertaken at Peking University First Hospital, Beijing, China. A total of 200 patients were divided equally into the MA twig alkaloid group or placebo group for a duration of 16 weeks. At week 16, the decline in HbA1c was 0.8% for the RM alkaloid group and 0.1% for the placebo group. Values in FBG and PBG are also significantly different.	[19]

Continued

Description of clinical study	Reference
This crossover and single-blind clinical study investigated the effect of MLE on the digestion and absorption of starch in 25 healthy subjects. For each subject, a ¹³ C-starch breath test was performed twice. Subjects ingested ¹³ C-abundant cornflakes either with the MLE (36 mg DNJ) or the placebo. A week later, each subject was given the opposite preparation. The overall dose recovery in percent was lower for the MLE test than for the placebo test. A significant decrease was detected 2 hours after the ingestion. A single dose of MLE, taken with a test meal, reduces starch digestion and absorption. This study was conducted at Poznan University of Medical Sciences in Poland.	[20]
At Duke University Medical Center, Durham, North Carolina, USA, a clinical study evaluated the effects of four doses of DH or DNJ on the pharmacokinetics and tissue levels of GAA (20 mg/kg) in 25 PD patients. AA alone resulted in an increase in total GAA and PP. When co-administered with DH, total GAA, and PP were further increased by 1.2- to 2.8-fold. Muscle GAA also increased.	[21]
Conducted at the Functional Food Centre, Oxford Brookes University, UK, a clinical study determined the effect of Reducose on healthy adults. The blood glucose and insulin responses when co-administered with 50 g maltodextrin of subjects given three doses of Reducose, a standardized MLE containing 5.0% of DNJ, in comparison with the placebo group. The MLE was found to significantly reduce total blood glucose and total insulin 120 minutes after ingestion of maltodextrin.	[22]
This randomized and double-blind clinical study at the University of Mississippi Medical Center, Jackson, USA, evaluated the hypoglycemic effect of a standardized MLE versus placebo given three times daily with meals. Subjects were patients with T2D and stable HbA1c. After 3 months, PPG was significantly decreased (16%) in the MLE group. There was no difference in HbA1c between the MLE and the placebo groups.	[23]
At Second Affiliated Hospital, Tianjin University, China, a clinical study investigated the effects of MLE on the GI of common dietary carbohydrates ingested by healthy volunteers. They were given 50 g of carbohydrate powder with or without 750 mg of MLE (7.5 mg of DNJ) dissolved in 150 ml of drinking water. Results showed that the consumption of MLE with sucrose, maltose, or maltodextrin can reduce their GI values.	[24]
A randomized controlled trial was conducted in Lambda Therapeutics Research Ltd. in Ahmedabad, India, to assess the effect of MA extracts on PPG and PPI responses in 72 healthy adults. MFE (1.5 g) and MLE (1.0 g) yielded a significant decline in PPG and PPI after 2 hours.	[25]
A clinical study at Khomein University of Medical Sciences, Iran, evaluated the effects of aqueous ethanol leaf extract of MN on FBG and HbA1c in diabetic patients. Patients in the treatment and control groups were given 3.0 ml extract or placebo three times a day. After 3 months, both FBG and HbA1c were significantly reduced in patients of the treatment group. This clinical trial showed that the MN leaf extract is effective in reducing blood glucose and HbA1c in diabetic patients.	[26]
This clinical study, conducted at the Oxford Brookes Centre for Nutrition and Health, UK, investigated the effects of Reducose (a standardized MLE with 4.5%–5.5% DNJ) on glycemic and insulinemic responses to 75 g sucrose in healthy subjects. Results showed that the addition of Reducose to sucrose resulted in significantly lower glycaemic and insulinemic responses compared to sucrose alone (placebo).	[27]
A clinical study performed at the Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, found that long-term (12 weeks) supplementation of DNJ-enriched MLE prevented the progression of diabetes in obese people with prediabetes or with early-stage diabetes by improving PPH, FPG, and HbA1c.	[28]
Two clinical trials were carried out at Lambda Therapeutics Research Ltd., Ahmedabad, India, to assess the efficacy of MFE for reducing PPG and PPI in healthy adults. Trial 1 used MFE in boiled rice, and MFE in rice porridge. MFE significantly decreased PPG by 23%–27% and PPI by 14%–35%. Trial 2 used MFE in boiled rice. MFE (0.37 g) significantly reduced PPG by 20% and PPI by 17%. These two trials showed that MFE in low doses can reduce PPG and PPI responses to meals rich in carbohydrates.	[29]
At Medical College Hospital and Peking Union Medical College, Beijing, China, a randomized, double-blind, and multi-center clinical trial was conducted to assess the efficacy of mulberry twig alkaloids for the treatment of T2D. HbA1c at week 16 was reduced by 0.8% in the treatment group and 0.1% in the placebo group.	[30]
This study, performed at Kashan University of Medical Sciences, Iran, was a randomized, double-blind, placebo-controlled trial, that involved 60 patients with T2D. The subjects were divided into 2 groups, receiving either MA extract (300 mg) or a placebo twice a day. Fasting blood samples were collected after 12 weeks. The extract group displayed a significant decrease in insulin and MDA, and a significant increase in HDL cholesterol.	[31]
At the Tokyo Institute of Technology, Japan, a randomized and double-blind clinical trial investigated the timing effects of MLE intake on PPG levels in young adults. 12 young adults participated and underwent 4 treatments, i.e., morning and evening placebo, and morning and evening MLE. EM blood glucose was significantly lower than EP. EM PPG was significantly lower than EP. MM PPI was significantly lower than MP. Overall, intake of MLE in the evening was more effective in improving glucose tolerance than in the morning.	[32]

AA = *α*-glucosidase alfa, AG = anhydroglucitol, AL = atherosclerotic lesions, DH = duvoglustat HCl, DNJ = 1-deoxynojirimycin, ELE = ethanol leaf extract, EM = evening mulberry, EP = evening placebo, FBG = fasting blood glucose, FPG = fasting plasma glucose, GA = glycated albumin, GAA = acid *α*-glucosidase, GI = glycemic indices, HbA1c = glycated hemoglobin, HDL = high-density lipoprotein, IGT = impaired glucose tolerance, LDL = low-density lipoprotein, MA = *Morus alba*, MDA = malondialdehyde, MFE = mulberry fruit extract, MLE = mulberry leaf extract, MM = morning mulberry, MP = morning placebo, PD = Pompe disease, PP = plasma protein, PPG = post-prandial glucose, PPH = post-prandial hyperglycemia, PPI = post-prandial insulin, SAP = stable angina pectoris, SMBG = self-monitoring blood glucose, T2D = type 2 diabetic, TG = triglyceride.

adipocytes [45]. The mechanism involved Akt-mediated insulin signaling pathway or AMP-activated protein kinase activation. A high-purity polysaccharide from mulberry leaf extract (MLE) (99.8% purity) exhibited anti-diabetic effects in streptozotocin-induced diabetic rats with effects equivalent to glibenclamide (GBC), an anti-diabetic drug [46].

DNJ, an alkaloid from MA leaves and twigs, is a potent *α*-glucosidase inhibitor and is effective in suppressing high blood glucose levels in human subjects, thus preventing T2D [4,9]. In diabetic mice, DNJ significantly decreased serum glucose and insulin levels, improved serum lipid contents, and reversed insulin resistance [47]. DNJ prevents the secretion of

Table 2. Clinical studies on other pharmacological properties of *Morus* species.

Effect	Description of clinical study	Reference
Hypolipidemic	An encapsulated MI leaf powder was evaluated for its hypolipidemic effect in comparison with GBC, an anti-diabetic drug. The clinical study was conducted at the Anantapur KM Hospital in Andhra Pradesh, India, and involved 24 mild T2D patients. The subjects were divided into two groups. The mulberry patients were given six capsules (two capsules after each meal, three times a day) each, amounting to 3 g/day for 30 days. The GBC patients were given one GBC tablet of 5 mg/day each for 30 days. Analysis of blood plasma and urine samples before and after treatment showed that the mulberry therapy significantly decreased serum cholesterol, TG, plasma free fatty acids, LDL-cholesterol, VLDL-cholesterol, plasma peroxides, and urinary peroxides concentration. However, HDL-cholesterol significantly increased.	[33]
	At Medical Corporation Kenshokai, Osaka, Japan, a clinical study evaluated the effects of DNJ-rich MLE on plasma lipid profiles in subjects. The mean serum TG level decreased from 312 to 269 mg/dl at week 6 and to 252 mg/dl at week 12. However, the differences were statistically not significant. Changes in blood biochemistry that included total cholesterol, LDL-cholesterol, and HDL-cholesterol were also not significant.	[34]
	At Chulalongkorn University, Bangkok, Thailand, a clinical trial evaluated the hypolipidemic effects of MA leaf tablets (each containing 1.3 mg of DNJ) on nondiabetic patients with mild dyslipidemia. TG was significantly decreased by 10% and 13% at weeks 4 and 8, respectively. At week 12, total cholesterol, TG, and LDL decreased by 4.9%, 14%, and 5.6%, respectively. However, HDL increased significantly by 20%. In conclusion, the MA leaf tablets were effective in reducing cholesterol levels and enhancing HDL in patients with mild dyslipidemia.	[35]
Cognitive enhancement	The cognitive enhancement effect of a standardized MLE was assessed at Khon Kean University in Thailand. The subjects involved 60 healthy middle-aged and elderly volunteers. They were given a daily dose of placebo or standardized MLE at 1.05 and 2.10 g for 3 months. The subjects who consumed MLE showed improved working memory and cognitive enhancement, without any discernable toxic effects. The possible mechanisms involved in working memory and cognitive enhancement require further studies.	[36]
	The effects of a single dose of mulberry milk on the cognitive function of children were investigated at Khon Kaen University, Thailand. The subjects comprised 46 healthy normal cognitive school-age children, were provided with 50 ml of milk containing 10 g of mulberry fruits or placebo milk. Attention, cognitive function, and working memory of the children were monitored. Improvement in attention and cognitive processing capabilities along with working memory of the school-age children affirmed the cognitive-enhancing potential of mulberry milk. The study attributed the reduction of cortisol (a stress hormone) as the possible underlying mechanism.	[37]
CHD attenuation	Conducted at First Hospital of Jilin University, Changchun, China, a clinical study reported that DNJ from MI leaves ameliorated SAP in patients with CHD and pleuritis syndrome by improving antioxidant and anti-inflammatory capacities. Other improvements were in angina-free walking distance and in symptoms such as chest pain, chest tightness, shortness of breath, emotional distress, and other clinical symptoms associated with SAP.	[38]
	A clinical study conducted at First Hospital of Jilin University in Changchun, China, reported that DNJ extracted from MA leaves attenuate AL in patients with CHD by improving serum lipid profile, and by reducing antioxidant, anti-inflammatory, and oxidative stress.	[39]
Anti-obesity	A clinical study conducted at the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand, investigated the optimal dose of DNJ in MLE. Another objective is to evaluate the efficacy and safety of the extract for glycemic control of obese persons with borderline diabetes. Results showed that the optimal dose for long-term administration of MLE was 12 mg of DNJ to reduce PPH without any side-effects except for some gastro-intestinal symptoms. Overall, MLE decreased FPG, glycated hemoglobin, and ameliorated insulin resistance.	[40]
Climacteric improvement	A randomized and double-blind clinical trial assessed the effects of MN leaf powder on symptoms and QL among climacteric women at the University Hospital of Federal University of Maranhão, Brazil. Results showed that climacteric symptoms and QL of the women improved following intake of 250 mg of MN leaf powder after 60 days.	[41]

AA = α -glucosidase, AG = anhydroglucitol, AL = atherosclerotic lesions, CHD = coronary heart disease, DH = duvoglustat HCl, DNJ = 1-deoxynojirimycin, FPG = fasting plasma glucose, GA = glycated albumin, GAA = acid α -glucosidase, GBC = glibenclamide, GI = glycemic indices, HbA1c = glycated hemoglobin, HDL = high-density lipid, LDL = low-density lipoprotein, MA = *Morus alba*, MI = *Morus indica*, MLE = mulberry leaf extract, MN = *Morus nigra*, PP = plasma protein, QL = quality of life, SAP = stable angina pectoris, T2D = type 2 diabetic, TG = triglyceride, VLDL = very low-density lipoprotein.

insulin and thus lowers fasting and post-prandial blood glucose levels associated with T2D [48]. Out of 21 clinical studies on anti-diabetic activities, 12 studies have been attributed to DNJ (Table 1).

Hypolipidemic

Mulberroside A was a stilbenoid isolated and purified from the ethanol root extract of MA while oxyresveratrol was produced from enzymatic conversion. Both compounds exhibited hypolipidemic effects in rats on a high-cholesterol diet. Rats orally treated with mulberroside A and oxyresveratrol

significantly decreased serum lipids, coronary artery risk index, and atherogenic index [49]. From the leaf of MA, a benzofuran derivative, a flavonoid, and an alkaloid displayed potent lipolytic activity in 3T3-L1 cells with values from 15.4% to 21.2% [43]. Rutin and quercetin-3-*O*- β -D-glucoside, two anti-diabetic flavonoids from the fruit of MA, reduced lipid accumulation in adipocytes [45].

Anti-obesity

The ability of MLE to suppress obesity and reduce visceral adipose tissues has been attributed to polyphenols

such as quercetin, kaempferol, rutin, caffeic acid, and chlorogenic acid [6]. From MLE, 2',7-dihydroxy-4'-methoxy-8-prenylflavan (flavan), isobavachalcone, and morachalcone B (chalcones) inhibited 3T3-L1 preadipocytes with IC_{50} values of 37, 43, and 48 μ M, respectively [50]. A pectic polysaccharide from MFE, named JS-MP-1, displayed an anti-obesity effect by inhibiting pre-adipocytes *via* reducing fat cells and adipose tissue [51].

Cognitive enhancement

Mulberrofuran G (2.13 and 9.72 μ M) and albanol B (2.47 and 1.39 μ M) from the root bark of MA possessed strong acetylcholinesterase and butyrylcholinesterase inhibitory activities, respectively [52]. These activities showed their ability to treat cognitive dysfunction associated with Alzheimer's disease (AD). Among four moracins isolated from the root of MA, the inhibition of BACE1, a beta-secretase enzyme in AD, moracin S was the strongest [53].

CHD attenuation

CHD is a common cardiovascular disease that causes human disability and death [54]. Among the various symptoms of CHD are angina pectoris, blood stasis syndrome, and atherosclerosis [38,39]. The underlying mechanisms of CHD are associated with inflammatory stress responses [55]. Compounds in *Morus* species that possess anti-inflammatory properties include DNJ and oxyresveratrol. DNJ, the main component in MA alkaloid tablets, possessed anti-inflammatory properties [56]. The alkaloid checked inflammation *via* regulation of mitogen-activated kinase signaling. DNJ markedly down-regulated interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) cytokine levels in lipopolysaccharide (LPS)-induced RAW 264.7 and bone marrow-derived macrophage cells. Oxyresveratrol, a stilbenoid, is another ingredient of MA that exerts anti-inflammatory activity *via* inhibition of leukocyte migration, and involvement of mitogen-activated ERK (MEK)/extracellular signal-regulated kinase (ERK) signaling [57]. Oxyresveratrol from MA also inhibited LPS-induced translocation of nuclear kappa B and cyclooxygenase-2 activity in RAW 264.7 cells [58,59]. The anti-inflammatory activity of oxyresveratrol has also been reported in RAW 264.7 cells, Jurkat leukemic T cells, and C28/I2 chondrocytes [60]. Quercetin 3-(6-malonylglucoside), a flavonol from MLE, attenuated atherosclerosis in low-density lipoprotein (LDL) receptor-deficient mice [61]. Among 36 compounds from the twig of MA, albanin D and 3-methyl-1-phenyl-1,3-butadiene exhibited the strongest anti-inflammatory activity of 4.1 and 2.2 μ M by inhibiting NO production in RAW 264.7 cells [62]. The potent anti-inflammatory activity of prenylated flavonoids from the root of MA and MN has been reported [63]. Noteworthy is kuwanon C with an IC_{50} value of 1.7 μ M. Albanol, an arylbenzofuran derivative from the root bark of MA, had the strongest anti-inflammatory effects towards RAW 264.7 cells, followed by sanggenon B and sanggenon D [64].

CONCLUSION

Objectives of clinical studies on MA include the effective dosage, duration, timing, and administration.

Materials used include mulberry tea, MLE powder, and confections containing enriched compounds such as DNJ, and standardized extract, e.g., reducose. Subjects are children, middle-aged adults, and elderly people, including people with CHD, impaired glucose tolerance (IGT), Pompe disease (PD), dyslipidemia, and climacteric symptoms. Some clinical studies on MA are designed to compare diabetic patients, people with dyslipidemia, and healthy or nondiabetic volunteers. Diabetic patients include post-prandial pre-diabetic, and borderline subjects. Placebo groups serve as controls. Further research is needed on the anti-diabetic mechanisms of mulberry leaves at the molecular level, which may involve multiple pathways. While most clinical trials have shown that mulberry leaves regulate blood glucose and lipid metabolism, research focusing on the safety of mulberry leaves is lacking. Studies are therefore needed to understand the distribution, absorption, metabolism, and excretion of mulberry compounds.

AUTHOR CONTRIBUTIONS

The author made substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published, and agree to be accountable for all aspects of the work. The author is eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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