Journal of Pharmacognosy and Phytochemistry
Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2020; 9(2): 2445-2451
Received: 19-11-2019
Accepted: 23-12-2019

Palvi Sharma
Ph.D. Scholar, Division of Sericulture, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, India

Arti Sharma
Ph.D. Scholar, Division of Sericulture, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, India

Jyoti Thakur
Ph.D. Scholar, Division of Sericulture, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, India

Murali S
Regional Sericultural Research Station, Central Silk Board, Miran Sahib, Jammu, Jammu and Kashmir, India

Kamlesh Bali
Associate Professor, Division of Sericulture, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, India

Corresponding Author:
Palvi Sharma
Ph.D. Scholar, Division of Sericulture, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, India

Mulberry as a Life Savior - A Review

Palvi Sharma, Arti Sharma, Jyoti Thakur, Murali S and Kamlesh Bali

Abstract
Plants play an important role in well-being of human beings and have been witnessed by their presence in the Rigveda and Ayurveda. Among those plants, *Morus* spp. is the one having versatile nature because of the presence of numerous phytochemicals in its different parts and also termed as 'Kalpavrishka'. Mulberry (*Morus* spp.) belongs to family Moracea and is widely planted in Asia. Although *Morus* spp. are the primary food of silkworm, *Bombyx mori* L. widely grown for rearing of silkworm. A wide range of the phytochemicals present in the leaves, fruit, root and wood of *Morus* because of which they possess wide range of biological functions (Antioxidant, anti-diabetic, anti-obesity, anticancer, antibacterial, antiviral, crypto protective and neuroprotective activities etc.). This review reveals the wide range of important life savior pharmacological properties of mulberry plant.

Keywords: Mulberry, Phytochemicals, Pharmacological properties, *Morus* spp., Biological functions

Introduction
Medicinal plants play an important role in Indian Ayurveda system of medicine and many active compounds were isolated from the plants by researchers which used as medicines. These active compounds are chemically in nature which is known as phyto-chemical or secondary plant products. Mulberry plant is one of conventional herbs which are used in medicine from centuries ago due to its chemical composition and pharmacological functions [9]. Mulberry is a fast growing woody perennial plant belongs to the family Moraceae and the genus *Morus* that contains more than 15 species of deciduous plants. The major ones include *Morus Alba*, *Morus indica*, *Morus nigra*, *Morus rubra*, *Morus australis*, *Morus atropurpurea*, *Morus cathayana*, *Morus notabilis* and *Morus mesozygia* [56]. Mulberry is found in a wide range of climatic, topographical and soil conditions, and it is widely distributed, from temperate to subtropical regions of the Northern hemisphere to the tropics of the Southern hemisphere. Since the ancient Chinese 'Material Medica' describes many medicinal benefits of mulberry, the potential nutritional and medicinal values of mulberry have attracted increasing research interest. Recent studies have demonstrated the nutritional value and health benefits associated with mulberry consumption [72].

Mulberry foliage is valued as the primary food for silkworms, supporting the silk industry for centuries [29]. The silkworm eats only mulberry leaves to make its cocoon, through which silk is produced, and there is a high correlation between the leaf protein content and the efficiency of cocoon production [45]. Various amino acids like threonine, valine, methionine, leucine, phenylalanine, lysine, histidine, and arginine found in mulberry leaves that are needed for silkworm growth. It is well established that the growth of silkworms, cocoon production and raw silk quality depends on the quality of mulberry leaves, which in turn is closely related to the plant varieties, environmental conditions, and cultivation practice [42]. Being nutritious, palatable, non-toxic and due to its ability to improve milk production can be used as fodder to dairy animals [6]. The high crude protein content and organic matter digestibility of mulberry leaves are superior to most tropical grasses commonly used as cattle feed [70]. In Traditional Chinese Medicine (TCM), leaves, fruits, and bark of *M. Alba* have long been used to treat fever, protect liver damage, improve eyesight, strengthen joints, facilitate discharge of urine, and lower blood pressure [9]. In Korea and Japan, mulberry leaves consume as an anti-hyperglycemic supplement to diabetic patients [34]. Mulberry leaves are effective against high blood pressure and hangover from alcohol [45]. In East and Southeast Asia, the drinking of mulberry tea is gaining popularity. The tea is rich in γ-aminobutyric acid (2.7 mg·g-1 dry weight) which is 10 times higher than that of green tea [66]. In Turkey and Greece, trees of *M. Alba* are grown for fruits rather than foliage [22]. The fruits are used to produce mulberry juice, jam, liquor, and canned mulberries. In China, the leaves of *M. Alba* are processed into tea while fruit juice is consumed as a health beverage [29]. Mulberry can be also use in mushroom Production [45]. In India, mulberry wood is made into sports equipment, furniture, household

utensils, and agricultural implements [16].

Studies reveals that the nutritional composition of mulberry leaves on dry weight basis that it contains 15.31- 30.91 *per cent* protein, 2.09- 7.92 *per cent* fat, 9.9-13.85 *per cent* crude fiber, 27.60- 43.6 *per cent* neutral dietary fiber (NDF) and 11.3-17.24 *per cent* ash contents [64]. Mulberry leaves containing sugars, rutin, quercetin, volatile oil, amino acid, vitamins and microelements that have so many pharmacological activities such as reducing blood glucose, ant hyperlipidemia, hypertensive, bacteriostatic and antivirus. Bio active compounds in different species of mulberry can enhance lifespan [69]. Different pharmaceutical properties of mulberry plants are reviewed by many scientists and they have reported that, many biochemical compounds such as Moran line, *Alba* furan, *Alba*nol, Morusin, Kuwanol, Calystegine and Hydroxymoricin are isolated from mulberry plants play an important role in pharmaceutical industry [3].

Photochemical studies have identified three flavonol glycosides, quercetin 3-(6 malonylglucoside), rutin and isoqercitrin, as major antioxidant compounds in the ethanol leaf extract of *M. Alba*[34] whereas by butanol extraction of leaf, two novel prenylflavanes and a glycoside, along with six known compounds, isoqercitrin, astragalin, scopolin, skimming, roseoids II and benzyl D-glucopyranoside were isolated [18]. Phytochemical studies of fruits of *Morus Alba* revealed that there are five anthocyanins [20] and 25 phenolic compounds [71] present in the fruit. From the root bark of *M. Alba*, polyhydroxylated alkaloids have been isolated, including 1-deoxynojirimycin (DNJ) and its derivatives [7]. The contents of DNJ is also present in the leaves of some varieties of mulberry, usually the younger leaves have higher DNJ content than the older leaves [27]. Other compounds identified from the root and root bark include terpenoids, flavonoids, stilbenoids and coumarins. Some bioactive compounds include mulberroside, resveratol and oxyresveratrol found in twig and stem of *M. Alba* [14].

Antioxidant activities of mulberry

Free radicals are chemical species possessing an unpaired electrons considered as fragments of molecules are generally very reactive. They are produced continuously in the cells either accidental by-products of metabolism or deliberately, for example, phagocytosis [2]. The potentially reactive derivatives of oxygen, ascribed as Reactive Oxygen Species (ROS) such as superoxide radical (O_2-), hydrogen peroxide (H_2O_2), hydroxyl radicals (OH) and alkoxyl radicals (RO) are routinely generated at low levels by plant cells. Under normal circumstances, production and destruction of ROS is well regulated in cell metabolism and there is equilibrium between the ROS generated and antioxidant enzymes present [21]. However, exposure of plants to adverse environmental conditions, ROS production will overcome scavenging systems favoring the ROS upsurge that culminate in oxidative stress [64]. In these conditions, ROS attack vital bio-molecules and disturb the cell metabolism and ultimately cell causes its own death. Plants have developed specific anti-oxidative defense enzymes including catalase, peroxidase, polyphenol oxidase, ascorbate peroxidase and glutathione reductase to control rapidly increasing ROS under various environmental stress conditions [63]. To avoid hazards associated with oxidative stress, antioxidants in the form of food supplement is required by the human body [56].

Antioxidant activity of *Morus* leaf was tested using silica gel column chromatography and isolated constituents were analyzed in vitro for antioxidant activity against DPPH and ABTS radicals [31]. Four flavonoids were isolated and all these compounds showed DPPH and ABTS radical scavenging activity [74]. Antioxidant potential of fruits of four mulberry species namely *Morus Alba, M. nigra, M. indica* and *M. laevigata* were studied and the result indicated higher total phenol and alkaloid contents having values [(880±7.20) - (1650±12.25)] mg/100g fresh weight and [(390±3.22)-(660±5.25)] mg/100g fresh weight respectively. Based on the results, it was concluded that mulberry fruit is a potential source of food diet and radical scavenging activity [30]. White mulberry stem bark, root bark, leaves and fruit content of methanolic extract was evaluated by *in vitro* standard method using spectrophotometer [37]. Among the extracts, stem bark showed highest antioxidant activity and hence, plant could serve as effective free radical inhibitor. Mulberry leaves treated with UV-C found to contain three different phytoalexins namely moracin C, moracin N and chalcomoracin and they are capable of scavenging superoxide anion [60]. Three different extracts of *M. nigra* (fruit juice, hydrochloric acid and polyphenols) on haemoglobin glycolysation, peroxidative damage to human erythrocytes were studied. All the three extracts inhibited haemoglobin glycolysation and haemolysis of human erythrocytes. Results suggest that *Morus nigra* has protective action against bio-membranes and biomolecules [43].

Hypoglycemic activity

Hypoglycemia is a condition that occurs when blood sugar level is too low in body. Diabetes mellitus is caused by the ineffectiveness of the insulin produced by pancreas [10]. The Diabetes mellitus is a group of metabolic disorders. It is characterized by high blood sugar (glucose) levels. This high blood sugar (glucose) levels is in response to the defects in insulin secretion, or its action, or both. The disease diabetes mellitus was first identified as a disease associated with "sweet urine," and excessive muscle loss in the ancient world. Increased levels of blood glucose (which may also called as hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine [32]. Due to inadequacy of insulin secreted by pancreas the concentration level of glucose increase in blood which harm many body systems in specifically the blood vessels and nerves [10].

The leaves of mulberry are one of the important herbal medicines used for the treatment of hyperglycemia. It was proved by experiments in animal models that mulberry leaf extract possess antihyperglycemic, antioxidant and antiglycation activities [48]. It is effective in modulating the nitric oxide synthase expression in the hypothalamus of streptazotocin treated rats [52]. *M. rubra* leaf extract exerts its antidiabetic activity in streptazotocin induced diabetic rats by decreasing the fasting glucose levels, glycosylated haemoglobin and increasing the plasma insulin and C-peptide levels [59]. A study on mulberry leaf extracts and found that mulberry leaf extract acts as a natural inhibitor of α glucosidase due to deoxynojirimycin (DNJ) and its derivatives [34]. 1- Deoxynojirimycin (DNJ), a known antidiabetic principle from mulberry has been shown to inhibit intestinal □-glucosidases resulting in reduction of blood glucose [26]. Fagomine, one of the components present in mulberry leaves is capable of inducing insulin secretion in isolated rat islet cells [67]. Moracin M, steppogenin-4'-O-ß-D-glucosiade and mullberroside A were also isolated from the root bark of *M. Alba* and all the three flavones showed hypoglycemic effect in alloxan induced diabetic mice[74]. The extracts from the root bark of mulberry tree contains some

components which showed hypoglycemic function, had defensive consequences on pancreatic β cells, obstruct their degeneration and decreased lipid peroxidation [10].

Anti -obesity activity

Obesity is defined as abnormal or extravagant fat accumulation that extant a risk to health. An obese person has accumulated so much body fat that it might have a negative effect on their health. Obesity is related with the diabetes, hypercholesterolemia, hyperlipidemia, hepatic steatosis, and atherosclerosis and decrease the amount of sugars absorbed has consequences for body weight [10]. Researchers suggested that mulberry extract might be beneficial in preventing human diabetes by suppressing intestinal alpha-glucosidase activities [8]. The air dried leaves and fruits of *ficus* and mulberry were examined in ethanol and hexane extract and evaluated against hyperlipidemia by estimating the rate limiting enzyme of cholesterol biosynthesis**.** A short term study on mice was conducted and exhibited an antagonistic action of mulberry extract on melanin concentrating hormone receptor, which help in decrease in body weight. They also suggested that ethanolic extract obtained from mulberry leaves showed anti-obesity action on diet-induced mice [10]. Quercetin, the quantitatively major flavonoids glycoside in mulberry leaves effectively suppressed the blood glucose levels [34]. Daily consumption of mulberry leaves improved hyperglycemia in diabetic rats and reduced oxidative stress in liver [39].

Hyperlipidemia activity

Hyperlipidemia is a characterized by excess cholesterol and fatty substances in the blood. Hyperlipidemia is a risk factor for heart disease. Diabetes mellitus is related with different kinds of lipid peculiarity. The lipaemia, cholesterol, especially LDL (low-density lipoprotein) and VLDL (Very-low-density lipoprotein) cholesterol are engaged in the growth of atherosclerosis and related abnormalities [5]. *Morus Alba* known for its medicinal properties and traditionally used for hypolipidemic activities. Consumption of MRBF-2 fraction of *M. Alba* L. root bark (70% alcohol extract) may act as potent hypocholesterolemic nutrient and inhibition of LDL antherogenic modifications and lipid peroxidase formation in hypocholesterolemic rats. Moracin present in mulberry leaves are capable of inhibiting lipid peroxidation that strongly indicates their role as scavenger. Mulberroside A prepared from ethanol root extract of *M. Alba* and its aglycone derivative (oxyresveratrol) produced from mulberroside A by enzymatic conversion have been evaluated for their anti-hyperlipidemic effects in two rat models [14]. Mulberry extract showed the hypolipidemic effects which elevate (Low density lipoprotein receptor) LDLR gene expression and the clearance proficiency of LDL (Low-density lipoprotein) and a decline in the lipid biosynthesis [10].

Anticancer activity

Many medicinal plants have anti-bacterial, anti-viral, anti-inflammatory, anti-cancer, immuno-stimulatory and antioxidant properties as well as compounds which effect specific organs. The methanolic extract of mulberry leaves shows efficient cytotoxic behavior against cancer cells. They identified many compounds like kuwanon S, 8 granilapigenin, ciclomulberrin, ciclomorusin, morusin, atalantoflavones, kaempherol with the action strong cytotoxic cell lines HeLa, MCF-7 and Hep3B. Anthocyanins isolated from *M. Alba* fruit showed inhibitory effect on invasion and migration of highly metastatic A549 human lung carcinoma cells in dose dependent manner [15] & [46]. Phenolic compounds from mulberry, *M. Alba* (L.) induces *in vitro* anticancer activity in hepatoma cells by cell cycle arrest at G2-M phase and inhibition of topo-isomerase II activity [49]**.** A new galactose binding lectin was also purified from *M. Alba* leaves with cytotoxic activity on human breast cancer (IC50-8.5 µg) and colon cancer cells (IC50-16 µg) [17]. The anthocyanins are a group of phenolic compounds with beneficial effects in reducing the risk of cardiovascular diseases and cancer because of its antioxidant, anti-inflammatory and chemopreventive properties [49]. Chalcones, a group of aromatic enones from plants, form the central core of a number of biologically important compounds. Investigation on ethanol extract of the leaves of *M. Alba* L. yielded two new chalcone derivatives, morachalcone B and C with potent cytotoxic effects [73]. Between the high content of anthocyanins, vitamin C, vitamin A, and various other polyphenolic and phytonutrient compounds, mulberries are absolutely packed with antioxidants. Antioxidants are the main line of defense against free radicals, which form a dangerous by-product of cellular metabolism and can damage healthy cells, causing them to mutate into cancerous ones. The diverse range of antioxidants found in mulberries means that they can neutralize these free radicals quickly before too much damage is done [32]. Prenylated flavanone, 7, 2′, 4′, 6'-tetrahydoroxy-6 geranyl flavanone separated from ethyl acetate extracts of *Morus Alba* root showed cytotoxic activity against hepatoma cells in rats with an IC50 of 52.8 mg/mL [40]. Further evaluation and clinical trials may reveal the therapeutic potential of *M. Alba* against cytotoxic cells that may help in finding a cheap and easily available source for treatment of cancer and decreasing invasiveness of cancerous cells. Stem bark of *M. wittiorum* was extracted with 95% ethyl alcohol, flavonoids and quercetins present in the bark exhibited selective cytotoxicity against human ovarian cancer and human gastric cancer [68].

Neuroprotective activity

Morus nigra owing to the presence of bioactive polyphenolic compounds such as anthocyanins, flavonoids, stilbene glycosides, lectins, oligosaccharides, unsaturated fatty acids, enzymes, and inhibitors possess pharmacological activities such as antihyperglycemic, anti-inflammatory, and neuroprotective effects [53]. Oxyreservatrol, a natural hydroxystilbene present in mulberry extracts, has been shown to have a neuroprotective effect in the case of neurodegenerative diseases due to oxidative damage such as Alzheimer's disease which is usually marked by cellular damage by high lipid peroxidation and increase in iron and aluminum [58]. Fruit extract of *M. nigra* has neuroprotective effect in inhibition of oxidative stress in the zebrafish brain owing to potent antioxidant properties of mulberry [23]. Mulberry fruit extract when tested against memory impairment and brain damage in animal model of vascular dementia, it was observed that mulberry fruit is potential natural cognitive enhancer and neuroprotectant [12]. Mulberry fruit contains the cyanidin-3-O-β-D-glucopyranoside which prevents the neuronal cell damage. They also suggest that mulberry fruit extracts having neuroprotective properties and prevent the cerebral ischemic damage caused by oxygen glucose deprivation (OGD) in PC12 cells [33].

Studies have demonstrated the beneficial effects of mulberry on the induction of an antioxidant defense system and improvement of memory deterioration in ageing animals [62]. The beneficial effect of mulberry extract (ME) rich in

phenolics and anthocyanins were evaluated. Six month old senescent- accelerated mice [SAMP8] and [SAMR1] were fed a basal diet supplement with 0.18 and 0.9 *per cent* mulberry extracts for 12 weeks. Mice fed with ME supplement showed significantly less amyloid beta protein and showed improved learning and memory ability. ME treated mice showed higher antioxidant enzyme activity and less lipid oxidation in both liver and brain as compared to control mice [75]. The neuroprotective effect of cyanidine- 3-glucoside (C3G) fraction from *M. Alba* was studied in oxygen deprivation and glutamate induced cell death in rat primary cortical neurons. C3G did not provide a protective effect against glutamate induced cell death, but provide protection against oxygen deprived cell death by maintaining the mitochondrial membrane potential [11]. Cholinesterases are key enzymes that play important roles in cholinergic transmission. Eight flavonoids including kuwanon U, kuwanon E, kuwanon C morusin, morusinol displaying cholinesterase inhibitory (both acetylcholine and butyrylcholine esterase) activity were isolated from the root bark of *M. lhou* L. [38].

Against gastrointestinal disorders

Mulberries are filled with nutrients that are important for our body, including iron, riboflavin, vitamin C, vitamin K, potassium, phosphorous, and calcium. They also contain a significant amount of dietary fiber and a wide range of organic compounds, including phytonutrients, zeaxanthin, resveratrol, anthocyanins, lutein, and various polyphenolic compounds. Dietary fiber can help to improve digestion by bulking up the stool, thereby speeding up the movement of food through the digestive tract, while also reducing occurrences of constipation, bloating, and cramping [32]. *M. Alba* extract significantly reduced the gastric mucosal injury in experimental rats induced by tween 20 and absolute ethanol with marked reduction in the leucocytes infiltration to submucosal layer [1]. The oral administration of methanolic extract from *M. nigra* fruits at a high dose (300 mg/kg) can protect gastric mucosa against acidified ethanol-induced acute gastric ulcer in female mice [50]. The mulberry consumption effectively prevents constipation in mice and is a promising therapeutic candidate for constipation. They also reported that mulberry treatment also increased the concentration of acetic, propionic, butyric valveric and isovaleric acids, increased the abundance of lactobacillus and bifidobacterium in faeces and decrease the abundance of helicobacter and prevotellaceae in faeces [28].

Antimicrobial activities

Infectious diseases accounts for high proportion of health problems in the world. Microorganisms have developed resistance to many antibiotics and as a result, immense clinical problems in the treatment of infectious diseases have been created. To solve this, researchers had identified many antimicrobial substances from medicinal plants including mulberry. The ethanolic extract of *Morus indica* leaf has antibacterial activity against *Staphylococcus aureus* and methalonic extract of *M. indica* leaf has antifungal activity against *Aspergillus niger* and *Penicillium* [51]. The methanolic extract of the bark of *M. mesozygia* as well as its constituents (cycloartocarpesin and different types of moracins) are used for the treatment of infections associated with microorganisms [41]. Kuwanon G isolated from the methanol root bark extract of *M. Alba* has been reported to exhibit antibacterial activity against oral pathogens such as *Streptococcus mutans*, *Streptococcus sanguis*, *Streptococcus sobrinus*, and *Porphyromonas gingivalis*, with the minimum inhibitory concentration (MIC) of 8 µg·mL-1 [54]. Prenylated flavonoids isolated from *M. Alba* showed antibacterial, antifungal and antiviral activities [20]. Flavonoids isolated from root bark of *M. Alba viz*., leachianone G and mulberroside C show potent antiviral activity (IC50 1.6 mg.Ml-1) and weak activity (IC50 75 mg. Ml-1) against herpes simplex type 1 virus (HSV-1). Chalcomoracin, a leaf phytoalexine of mulberry tree exhibited considerable antibacterial activity against methicillin-resistant *Staphylococcus aureus* [25].

Against skin diseases

Melanin is a complex polymer derived from the amino acid tyrosine. Melanin is responsible for determining skin color. Melanin is produced through a multistage chemical process known as melanogenesis, where the oxidation of amino acid tyrosine is followed by polymerization. The melanin pigments are produced in specialized group of cells known as melanocytes**.** Tyrosinase is a copper- containing enzyme present in plant and animal tissues that catalyzes the production of melanin and other pigments from tyrosine by oxidation. It is found inside melanosomes which are synthesized in the skin melanocytes. In humans, the tyrosine enzyme is encoded by the TYR gene. Tyrosinase inhibitors are more important in improving skin to prevent the overproduction of melanin [13]. Melanin protects from UV induced hyper pigmentation, wrinkling, melasma (Brown patches on skin) and cancer [56]. A number of natural tyrosinase inhibitors have been reported [36]. Among those, extracts from leaves and root barks of mulberry exhibited high inhibition on the DOPA oxidase activity and anti-tyrosinase activity [44]. Mulberroside F isolated from the methanol leaf extract of *M. Alba* exhibits anti-tyrosinase activity that is 4.5-fold stronger than kojic acid and has an inhibitory effect on melanin formation in melan-a cells (44). Oxyresveratrol exhibits an inhibitory activity that is 32-fold stronger than kojic acid [61]. *M. Alba* L. leaf extract exhibited potent inhibitory effects on mushroom tyrosinase, mammalian tyrosinase, and melanin synthesis in Melan-a cells [44]. The extract of mulberry (*M. Alba*) from leaves or root barks exhibited free radical scavenging and antioxidant activities thus, it may benefit for depigmentation [4]. TMBC, a chalcone from the stem of *M. nigra* modulated melanogenesis by inhibiting tyrosinase [76]. Topical applications of mulberroside A, oxyresveratrol, and oxyresveratrol-3-O-glucoside clearly caused de-pigmentation, reduced melanin indices, inhibited tyrosinase activity, and decreased melanin content in UV induced hyperpigmentation in guinea pig skin. Oxyresveratrol and oxyresveratrol-3-O-glucoside more potently inhibited melanogenesis than mulberroside A. This treatment decreased the expression of MITF gene, that are regulating the transcription of proteins involved in melanocyte pigmentation [55]. Mulberroside F isolated from mulberry leaves might be used as a skin whitening agent [13]. Mulberries also boast a high level of vitamin A and vitamin E, along with a range of carotenoid components like lutein, beta-carotene, zeaxanthin, and alphacarotene. All of these elements act as antioxidants that specifically affect the skin, tissue, hair, and other areas of the body where free radicals strike. Mulberries can aid in skin care, reduce the appearance of blemishes and age spots, and keep hair shiny and healthy by preventing the oxidative actions of free radicals [32].

Conclusion

Mulberry being the primary food for silkworm *Bombyx mori* L., supported the silk industry over centuries. Mulberry plant is also considered as the important traditional herbs widely used in medicine from centuries ago. Mulberry is rich in phenols (resveratrol, oxyresveratrol, chlorogenic acid, mulberroside, maclurin and moracins), anthocyanins (cyaniding-3-glucoside, cyaniding-3-rutinoside, geranium-3-glucoside), non-anthocyanin flavonoids(rutin, quercetin, kaempferol-3-rutinoside), alkaloids (DNJ, fagomine) and polysaccharides possess pharmacological properties including antioxidant, antiflammatory, anticarcinogenic, antibacterial, antiviral, anti-obesity, anti-apoptotic, anti-diabetic, neuroprotective activities. The Phytochemical composition varies with the species of *Morus* and the plant part use. However, human intervention studies on the pharmacological activities of mulberry fruits are limited. Therefore, future studies should explore the effect of mulberry fruit consumption on human health and elucidate the detailed compounds.

References

1. Abdulla MA, Ali HM, Ahmed KA, Noor SM, Ismail S. Evaluation of the anti-ulcer activities of *Morus Alba* extracts in experimentally induced gastric ulcer in rats. Biomedical Res. 2009; 20:35-39.
2. Ajitha M, Rajnarayana K. Indian Drugs. 2001; 38(11):545-553.
3. Andallu B, Suryakantham V, Srikanthi BL, Reddy GK. Effect of mulberry (*Morus indica* L.) therapy on plasma and erythrocyte membrane lipids in patients with type 2 diabetes. Clinica Chimica Acta. 2001; 314:47-53.
4. Andallu B, Varadacjaryulu N. Antioxidant role of mulberry (*Morus indica* L. cv. Anantha) leaves in streptozoticin- diabetic rats. Clinica Chimica Acta. 2003; 338:3-10.
5. Andallu B, Vinay Kumar AV, Varadacharyulu N. Lipid abnormalities in streptozotocin-diabetes: Amelioration by *Morus indica* L. cvSuguna leaves. International Journal of Diabetes Developing Countries. 2009; 29(3):123-128.
6. Arabshahi-Delouee S, Urooj A. Antioxidant properties of various solvent extracts of mulberry (*Morus indica* L.) leaves [J]. Food Chemistry. 2007; 102:1233-124.
7. Asano N, Oseki K, Tomioka E. N-containing sugars from *Morus Alba* and their glycosidase inhibitory activities [J]. Carbohydrate Res. 1994; 259:243-255.
8. Asano N, Yamashita T, Yasuda K, Ikeda K, Kizu H, Kameda Y, Kato A, Nash RJ, Lee HS, Ryu KS. Polyhydroxylated alkaloids isolated from mulberry trees (*Morus Alba* L.) and silkworms (*Bombyx mori* L.). Journal of Agriculture and Food Chemistry. 2001; 49:4208-4213.
9. Bae SH, Suh HJ. Antioxidant activities of five different mulberry cultivars in Korea [J]. LWT- Food Science and Technology. 2007; 40(6):955-962.
10. Bajpai Saurabh, Rao Bhaskara Vijaya A, Muthukumaran M, Nagalashmamma K. History and active pharmacokinetic principles of mulberry: a review. Journal of Pharmacy. 2012; 2(4):13-16.
11. Bhuiyan MIH, Kim HB, Kim SY, Cho KO. The neuroprotective potential of cyanidin-3-glucoside fraction extracted from mulberry following oxygen-glucose deprivation. The Korean Journal of Physiology & Pharmacology. 2011; 15:353-361.
12. Bihnen NI, Albin RL. The cholinergic system and Parkinson's disease. Behavioural Brain Research. 2011; 221(2):564-73.
13. Butt Sadiq Masood, Nazir Akmal, Sultan Tauseef M, Schroen Karin. *Morus Alba L*. nature's functional tonic. Trends in Food Science & Technology. 2008; 19(10):505-512.
14. CHAN Wei-Chiang Eric, LYE Phui-Yan, WONG Siu-Kuin. Phytochemistry, pharmacology, and clinical trials of *Morus Alba*. Chinese Journal of Natural Medicine. 2016; 14(1):0017-0030.
15. Colonna M, Danzon A, Delafosse P, Mitton N, Bara S, Bouvier AM *et al.* Cancer prevalence in France: time trend situation in 2002 and extrapolation to 2012. European Journal of Cancer. 2008; 44:115-122.
16. Datta RK, Sánchez MD. Mulberry for Animal Production. Mulberry cultivation and utilization in India [M]. FAO Animal Production Health Paper, 2002.
17. Deepa M, Priya S. Purification and characterization of a novel anti-proliferative lectin from *Morus Alba* L. leaves. Protein and peptide letters. 2012; 19(8):839-845.
18. Doi K, Kojima T, Makino M *et al*. Studies on the constituents of the leaves of *Morus Alba* L. [J]. Chemical & pharmaceutical bulletin. 2001; 49(2):151-153.
19. Du J, He ZD, Jiang RW. Antiviral flavonoids from the root bark of *Morus Alba* L. [J]. Phytochemistry. 2003; 62:1235-1238.
20. Du Q, Zheng J, Xu Y. Composition of anthocyanins in mulberry and their antioxidant activity [J]. J Food Compos Anal. 2008; 21:390-395.
21. Elfalleh W, Tlili N, Nasri N, Yahia Y, Hannachi H, Chaira N. Antioxidant capacities of phenolic compounds and tocopherols from *tunisian pomegranate* (*Punica granatum*) fruits. J Food Sci. 2011; 76:707-713.
22. Ercisli S, Orhan E. Chemical composition of white (*Morus Alba*), red (*Morus rubra*) and black (*Morus nigra*) mulberry fruits [J]. Food Chemistry. 2007; 103:1380-1384.
23. Erkekoglu P, Baydar T. Acrylamide neurotoxicity. Nutritional Neuroscience. 2014; 17(2):49-57.
24. Fang SH, Hou YC, Chao PD. Pharmacokinetic and pharmacodynamic and interactions of morin and cyclosporine. Toxicology and Applied Pharmacology. 2005; 205:65-70.
25. Fukai T, Kaitou K, Terada S. Antimicrobial activity of 2-arylbenzofurans from Morus species against methicillin-resistant *Staphylococcus aureus*. Fitoterapia. 2005; 76:708-11.
26. Hansawasdi C, Kawabata J. Alpha-glucosidase inhibitory effect of mulberry (*Morus Alba*) leaves on Caco-2. Fitoterapia. 2006; 77:568-73.
27. Hu XQ, Jiang L, Zhang JG. Quantitative determination of 1-deoxynojirimycin in mulberry leaves from 132 varieties [J]. Industrial Crop Production. 2013; 49:782-784.
28. Hu Gen-Teng, Wen Peng, Fu Hui-Zhan, Lin Guang-Yue, Liao Sen-Tai, Zou Yu-Xiao. Protective effect of mulberry (*Morus atropurpurea*) fruit against diphenoxylate-induced constipation in mice through the modulation of gut microbiota. Food and Function. 2019; 10:1513-1528.
29. Huo Y, Sánchez MD. Mulberry for Animal Production. Mulberry cultivation and utilization in China [M]. *FAO* Anim Prod Health Paper, 2002.
30. Imran M, Khan H, Shah M, Khan R, Khan F. Chemical composition and antioxidant activity of certain *Morus*

species. Journal of Zhejiang University Science. 2011; 11:973-980.
31. Jiang YL, Piao HS, Li G. Study on antioxidant activity of constituents from mulberry leaf. Zhong Yao Cai. 2008; 31(4):519-522.
32. Kadam Ashok Rutuja, Dhumal Dattatray Nivedita, Khyade Bhimasha Vitthalrao. The Mulberry, *Morus Alba* (L.*)*: The Medicinal Herbal Source for Human Health. International Journal of Current Microbiology and Applied Sciences. 2019; 8(4):2941-2964.
33. Kang Tong Ho, Jin Young Hur, Hyun Bok Kim, Jong Hoon Ryu, Sun Yeou Kim. Neuroprotective effects of the cyanidin- 3-O-beta-d-glucopyranoside isolated from mulberry fruit against cerebral ischemia. Neuroscience Letters. 2006; 391(3):122-126.
34. Katsube T, Imawaka N, Kawano Y, Yamazaki Y, Shiwaku K, Yamane Y. Antioxidant flavonol glycosides in mulberry (*Morus Alba* L.) leaves isolated based on LDL antioxidant activity. Food Chemistry. 2006; 97:25-31.
35. Katsube T, Yamasaki M, Shiwaku K, Ishijima T, Matsumoto I, Abe K *et al.* Yamasaki Y. Effect of flavonol glycoside in mulberry (*Morus Alba*) leaf on glucose metabolism and oxidative stress in liver in diet-induced obese mice. J Sci Food Agri. 2010; 90:2386-2392.
36. Khan KM, Maharvi GM, Abbaskhan A, Hayat S, Khan MTH, Makhmoor T *et al.* Three tyrosinase inhibitors and antioxidant compounds from *Salsola foetida*. Helvetica Chimica Acta. 2003; 86:457-464.
37. Khan MA, Rahman AA, Islam S, Khandokhar P, Parvin S, Islam MB *et al.* Rashid A comparative study on the antioxidant activity of methanolic extracts from different parts of *Morus Alba* L. (*Moraceae*). BMC Research Notes. 2013; 6:24.
38. Kim GN, Jang HD. Flavonol content in the water extracts of the mulberry (*Morus Alba)* leaf and their antioxidant capacities. J Food Sci. 2011; 76:869-73.
39. Kim GN, Kwon YI, Jang HD. Mulberry leaf extract reduces postprandial hyperglycemia with few side effects by inhibiting α-glucosidase in normal rats. Journal of Medicinal Food. 2011; 14:712-717.
40. Kofujita H, Yaguchi M, Doi N, Suzuki K. A novel cytotoxic prenylated flavonoid from the root of *Morus Alba*. J Insect Biotechnol Sericol. 2004; 73:113-116.
41. Kuete V, Fozing DC, Kapche WFGD, Mbaveng AT, Kuiate JR, Ngadjui BT *et al.* Antimicrobial activity of the methanolic extract and compounds from *Morus mesozygia* stem bark. Journal of Ethnopharmacology. 2009; 124:551-5.
42. Kumar RV, Kumar D, Pher R. Varietal influence of mulberry on silkworm, *Bombyx mori* L. growth and development [J]. Int J Adv Res. 2014; 2(3):921-927.
43. Lee CY, Cheng HM, Sim SM. Mulberry leaves protect rat tissues from immobilization stress-induced inflammation. Biofactors. 2007; 31(1):25-33.
44. Lee SH, Choi SY, Kim H, Hwang JS, Lee BG, Gao JJ *et al.* isolated from the leaves of *Morus Alba* inhibits melanin biosynthesis. Biological and Pharmaceutical Bulletin. 2002; 25:1045-8.
45. Machii H, Koyama A, Yamanounchi H. Mulberry for Animal Production. Mulberry breeding, cultivation and utilization in Japan [M]. FAO Anim Prod Health Paper, 2002.
46. Martin-Moreno JM, Soerjomataram I, Magnusson G. Cancer causes and prevention: A condensed appraisal in Europe in 2008. European Journal of Cancer. 2008; 44:1390-1403.
47. Middleton JRE, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. Pharmacol Rev. 2000; 52:673-751.
48. Naowaboot J, Pannangpetch P, Kukongviriyapan V, Kongyingyoes B, Kukongviriyapan U. Antihyperglycemic, antioxidant and antiglycation activities of mulberry leaf extract in streptazotocin induced chronic diabetic rats. Plant Foods for Human Nutrition. 2009; 64:116-21.
49. Naowaratwattana W, De-Eknamkul W, De Mejia EG. Phenoliccontaining organic extracts of mulberry (*Morus Alba* L.) leaves inhibit HepG2 hepatoma cells through G2/M phase arrest, induction of apoptosis, and inhibition of topoisomerase IIa activity. Journal of Medicinal Food. 2010; 13:1045-56.
50. Nesello LAN, Beleza MLML, Mariot M, Mariano LNB, de Souza P, and Campos a *et al.* Gastroprotective Value of Berries: Evidences from Methanolic Extracts of *Morus nigra* and *Rubus niveus* Fruits. Gastroenterol. Res. Pract. 2017; 70(8):96-97.
51. Niratker Ravi Chaitali, Preeti and Malti. Antimicrobial activity of leaf extract of *Morus indica* (Mulberry) from Chhattisgarh, Pelagia Research Library. 2015; 5(1):28-31.
52. Oh BK, Oh KS, Kwon KI, Ryu SY, Kim YS, Lee BH. Melanin-concentrating hormone-1 receptor antagonism and antiobesity effects of ethanolic extract from *Morus Alba* leaves in diet-induced obese mice. Phytotherapy Research. 2010; 24(6):919-923.
53. Padilha MM, Vilela FC, Rocha CQ, Dias MJ, Soncini R, dos Santos MH *et al.* Anti-inflammatory Properties of *Morus nigra* leaves. Phytotherapy Research. 2010; 24:1496-00.
54. Park KM, You JS, Lee HY. Kuwanon G: an antibacterial agent from the root bark of *Morus Alba* against oral pathogens [J]. Journal of Ethnopharmacology. 2003; 84:181-185.
55. Park KT, Kim JK, Hwang D, Yoo Y, Lim YH. Inhibitory effect of mulberroside A and its derivatives on melanogenesis induced by ultraviolet B irradiation. Food and Chemical Toxicology. 2011; 49:3038-45.
56. Pihlanto A, Akkanen S, Korhonen HJ. ACE-inhibitory and antioxidant properties of potato (*Solanum tuberosum*). Food Chemistry. 2008; 109:104-112.
57. Priya Sulochana. Medicinal Values of Mulberry- An Overview. Journal of Pharmacy Research. 2012; 5(7):3588-3596.
58. Rodrigues EL, Marcelino G, Silva GT, Figueiredo PS, Garcez WS, Corsino J *et al.* Nutraceutical and medicinal potential of the *Morus* sp. in metabolic dysfunctions. International Journal of Molecular Sciences. 2019; 20:301-03.
59. Sachdewa A, Khemani LD. Effect of *Hibiscus rosasinensis* Linn ethanol flower extract on blood glucose and lipid profile in streptozotocin induced diabetes in rats. Journal of Ethropharmacology. 2003; 89:61-6.
60. Sharma R, Sharma A, Shono T, Takasugi M, Shirata A, Fujimora T *et al.* Mulberry moracins: Scavangers of UV-stress generated free radicals. Biosci Biotechnol Biochem. 2001; 65(6):1402-1405.

61. Shin NH, Ryu SY, Choi EJ. Oxyresveratrol as the potent inhibitor on dopa oxidase activity of mushroom tyrosinase [J]. Biochem Biophys Res Commun. 1998; 243:801-803
62. Shih PH, Chan YC, Liao JW, Wang MF, Yen GC. Antioxidant and cognitive promotion effects of anthocyanin-rich mulberry (*Morus atropurpurea* L.) on senescence-accelerated mice and prevention of Alzheimer's disease. Journal of Nutritional Biochemistry. 2010; 21:598-605.
63. Singhania N, Puri D, Madhu SV, Sharma SB. Assessment of oxidative stress and endothelial dysfunction in Asian Indians with type 2 diabetes mellitus with and without macroangiopathy. QJM: An International Journal of Medicine. 2008; 101(6):449-455.
64. Sreelatha S, Padma PR. Antioxidant activity and total phenolic content of *Moringa oleifera* leaves in two stages of maturity. Plant Foods and Human Nutrition. 2009; 64:303-311.
65. Srivastava S, Kapoor R, Thathola A, Srivastava RP. Mulberry *(Morus Alba)* leaves as human food: a new dimension of sericulture. International Journal of Food Science and Nutrition. 2003; 54:411-416.
66. Suttie JM. *Morus Alba* L. Grassland Species Profiles [M]. Rome: Food and Agriculture Organization (FAO), 2005.
67. Taniguchi S, Asano N, Tomino F, Miwa I. Potentiation of glucose induced insulin secretion by fagomine, a pseudosugar isolated from mulberry leaves. Hormonic and Metabolic Research. 1998; 30:679-83.
68. Tan YX, Liu C, Chen R. Phenolic constituents from stem bark of *Morus wittiorum* and their anti-inflammation and cytotoxicity. Zhongguo Zhong Yao Za Zhi. 2010; 35(20):2700-2703.
69. Venkatesh Kumar R. Seema Chauhan. Mulberry: Life enhancer. Journal of Medicinal Plants Research. 2008; 2(10):271-278.
70. Vu CC, Verstegen MWA, Hendriks WH. The nutritive value of mulberry leaves (*Morus Alba*) and partial replacement of cotton seed in rations on the performance of growing *Vietnamese* cattle [J]. Asian-Australasian Journal of Animal Sciences. 2011; 24(9):1233-1242.
71. Wang Y, Xiang L, Wang C. Antidiabetic and antioxidant effects and phytochemicals of mulberry fruit (*Morus Alba* L.) polyphenol enhanced extract [J]. PLoS ONE. 2013; 8(7):711-44.
72. Wen Peng, Hu Teng-Gen, Linhardt J. Robert, Liao Sen-Tai, Wu Hong and Zou Yu-Xiao. Mulberry: A review of bioactive compounds and advanced processing technology. Trends in Food Science and Technolgy. 2019; 83:138-158.
73. Yang X, Yang L, Zheng H. Hypolipidemic and antioxidant effects of mulberry (*Morus Alba* L.) fruit in hyperlipidaemia rats. Food Chemistry and Toxicology. 2010; 48:2374-9.
74. Zhang M, Chen M, Zhang HQ, Sun S, Xia B, Wu FH. In vivo hypoglycemic effects of phenolics from the root bark of *Morus Alba*. Fitoterapia. 2009; 80(8):475-477.
75. Zhang W, Han F, Duan C. HPLC-DAD-ESI-MS/MS analysis and antioxidant activities of non-anthocyanin phenolics in mulberry (*Morus Alba* L.). Journal of Food Science. 2008; 73(51):512-518.
76. Zhang X, Hu X, Hou A, Wang H. Inhibitory effect of 2,4,2',4'-tetrahydroxy-3-(3-methyl-2-butenyl)-chalcone on tyrosinase activity and melanin biosynthesis. Biological and Pharmaceutical Buletin. 2009; 32:86-90.