



## MORUS ALBA'S PHARMACOLOGICAL AND THE PHYTOCHEMISTRY ACTIVITY

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**Article History: Received:** 03.04.2023

**Revised:** 13.05.2023

**Accepted:** 23.06.2023

### Abstract

This review article provides an overview of the pharmacological and plant chemistry of the alba species of Morus. Morus alba (mulberry) is a medicinal plant which belongs to family Moraceae. It has been used as a medicine since ages due to its various therapeutic properties. Various mulberry plant components have been shown to have hepatoprotective, anti-oxidant, cardiovascular, anti-obesity, anti-inflammatory, anti-cancer, anti-microbial, anti-mutagenic, anti-diabetic and nephroprotective properties. Other medicinal effects of mulberry include anti-platelet, anti-depressant, anti-asthmatic, immune modulatory, gastrointestinal and cholesterol lowering effects. The plant contains various phytochemicals such as flavonoids, alkaloids, anthocyanins, tannins, glycosides, terpenoids, steroids, phytosterols, saponins, benzofuran derivatives. This phytopharmacological study indicates that Morus alba can be used as a of therapeutic in future use.

**Key words:** Morus alba, Moraceae, phytochemicals, pharmacological properties..

### Introduction:

Phytochemical rich plants have been used to cure various diseases for thousands of years because natural products are less toxic and have less side effects [1]. Mulberry is one of the widely used medicinal plant. M. alba belongs to family Moraceae and genus Morus. It is widely known as white mulberry. It is commonly known as Tut in India. A mulberry tree can grow to a height of 10 to 20 metres [2]. It is originated from China. Mulberry possesses many pharmacological properties and has low toxicity. It has been widely used in traditional Chinese medicine since 659 AD [3]. The root bark, stem, fruits and leaves are used for medicinal purpose. M. alba leaves are used to feed silkworms [4].

### Habitats:

They are raised in Asia's subtropical nations, including China, India, Japan, and

Korea. They are also made in some other continents, including Africa and North America. Nine of the fourteen species of M. alba are found in Asia, while the other five have only recently been identified on other continents [5].

### Description:

Fast-growing M. alba is a shrub with a straight, cylindrical trunk that can grow up to 35 metres high and 1.8 metres in diameter. Bark that is hard and cracked and oozes white latex is greyish brown in colour [6] with two rows of oval leaves and a straightforward trilobal, dentate, palm with three veins at the base, the stem is lateral, scaly, and coral. Flowers with four loose, scale-like petals are greenish. Male flowers have four stamens and are arranged in racemes that resemble catkins [7]. Two styles, one ovule, one ovary blockage, long or short spikes on female flowers, fan-shaped with ovules. Ovarian

syncarpous fruit with up to 5 cm long, fleshy perianths that encase several drupes [8].

### **Bioactive Compounds in Mulberry**

#### **• Flavonoids**

Flavonoids are a class of plant metabolites which are found in deeply pigmented fruits and vegetables. *Morus alba* is also one of them. Most flavonoids are replaced by phenyl and geranyl groups. Different types of flavonoids are formed by cyclization. [10]. The outermost layer of foliage, peels of fruit, and bark contain flavonoids. Mulberry leaves contain flavanols, which are a type of flavonoids. Mulberry leaves were used to extract the caffeoylquinic acid derivatives neochlorogenic acid, chlorogenic acid, crypto chlorogenic acid, caffeoylquinic acid isomer, and caffeoylquinic acid glucoside. Numerous pharmacological activities of flavonoids include hepatoprotective, carcinogenic effects, antiallergenic, antithrombotic, antiviral, and anti-inflammatory [11].

#### **Alkaloids**

In 1804, alkaloid morphine was extracted from opium poppy. Alkaloids are compounds, made up of nitrogen atoms, sulfur, oxygen, phosphate, chlorine etc. They exhibit many pharmaceutical activities like anti-cancer, anti-malarial, etc. [12]. Alkaloid is found in *M. alba* fruit; it is used as antifeedant. Ripened fruit has higher levels of alkaloids because it is a secondary metabolite [13].

#### **Anthocyanins:**

Anthocyanins are pH dependent compounds. Mulberry fruits contains Resveratrol which is a type of Anthocyanin, it protects against the chances of strokes by altering molecular pathways in the blood vessels; their liability to damage by reducing angiotensin activity (a systemic hormone causing shrinking of the blood vessels that would increase lead to high blood pressure) while boosting the buildup of vasodilator hormone [14]. Mulberry fruit contains anthocyanins in the form of

polyphenol with antioxidant property and many other medicinal properties. 20 types of anthocyanins were extracted from Mulberry Fruit Extract (MFE). Out of the 20 variations found, Cyanidin 3-O-glucoside (301.75 mg/g of mulberry anthocyanin extract) is the primary anthocyanin isolated from *M. alba* fruit and has anticancer and anti-diabetic activities [13].

#### **Phenolic acids:**

Food-polyphenolic constituents derived from plants are the most popular phytochemicals. They are better antioxidants than vitamins E or C. they help in preventing diseases. They are present in fruits and vegetables. They are secondary, aromatic plant metabolites that are present in a wide variety of plants. Polyphenolic acids have a major impact on food quality and their palatability [12, 15].

#### **Pharmacological Review:**

##### **Anti- obesity:**

Obesity is defined as a disorder involving excessive body fat that causes chronic illness. An obese person has so much body fat stored that it raises the possibility of serious health issues. Obesity slows sugar absorption and increases the risk of developing insulin resistance, high cholesterol levels, elevated cholesterol levels, steatosis of the liver, and atherosclerotic [16]. According to an experimental study on mice, it was observed that mulberry extract works against melanin concentrating hormone receptor, which reduces body fat. *M. alba* leaves contain ethanolic extracts which has anti-obesity action on diet-induced mice [17].

##### **Antioxidant properties:**

Ethanol fruit extract from various varieties of mulberry possess different antioxidant properties. Stronger than vitamin C at scavenging free radicals, anthocyanins are excellent antioxidant agents. High levels of anthocyanin are seen in ripened *M. alba* fruit. Aqueous methanol leaf extracts of mulberry exhibit greater values than that of fruits in terms of overall phenolic

content (TPC), free radical scavenging (FRS), ferric decreasing power (FRP), and ferrous ion chelating (FIC) [18]. "The ranking is of the order: developing leaves > young leaves ~ mature leaves > mature fruits". Mulberry exhibits the benefits of drying. Potential FRS activity can be seen in the root bark of *M. alba* and the activity of xanthine oxidase and peroxidation of lipids are inhibited. In rats, Water extract of mulberry root bark shows antioxidant properties in assays FeCl<sub>2</sub>-ascorbic acid-induced lipid peroxidation. Methanol extracts increases FRS effect of mulberry branches, roots and leaves (>70%). *M. alba* fruits displays the highest FRS effect [19].

#### **Antibacterial activity:**

Methanol and ethyl acetate extract of mulberry is made from its leaf, fruit, and stem part. This extract contains many phytochemicals. Testing for antibacterial action in plants is done using the Kirby-Bauer disc diffusion method. Gram-positive bacteria such *Bacillus* sp., *S. aureus*, and *E. faecalis* were observed to be prevented from spreading by mulberry leaf extract in methanol at 100% concentration [20]. *E. faecalis* had the biggest suppression zone, followed by *S. aureus* and *Bacillus* sp. Depending on concentration, diluted extract (at 6.25% concentration) demonstrated reduction of bacterial spread. *S. aureus* and *E. faecalis* cannot spread when mulberry leaf extract is used. Gram-negative bacteria and fungus are both inhibited by the ethanolic extract of mulberry leaves. The antibacterial properties of mulberry fruit and stem have also been investigated. Methanolic extract from fruit and stem of mulberry have lesser antibacterial activity as compared to the methanolic extract from its leaf [21]. Kuwanon G is a type of phytochemical which is found in the methanol root bark extract of *Morus alba*. It exhibits antibacterial action against oral pathogens such *Streptococcus mutans*, *Streptococcus sanguis*, *Streptococcus sobrinus*, and *Porphyromonas gingivalis* at

the minimum inhibitory concentration, or MIC, of 8 gmL. Mulberry prenylated flavonoids had antiviral, antifungal, and antibacterial activities. Leachianone G and mulberroside C, two flavonoids contained in the root bark of mulberries, have significant antiviral effects (IC<sub>50</sub> = 1.6 mg. Ml-1) and weak effects (IC<sub>50</sub> = 75 mg. Ml-1) against the herpes simplex type 1 virus (HSV-1). A phytoalexine found in mulberry leaves known as chalconoracin exhibits antibacterial properties against methicillin-resistant *S. aureus* [22].

#### **Anti- Diabetic Activity:**

The antihyperglycemic and antioxidant activities of mulberry leaf were investigated in an experimental investigation using male Wistar rats that had developed diabetes as a result of the drug streptozotocin (STZ). The leaves of *M. alba* were found to decrease excessive levels of peroxidation of lipids and catalase (CAT) effects in RBCs in diabetic mice (48% and 33%, respectively). Branch bark extract (BBE) lowers elevated serum INS levels and manages dyslipidemia in diabetic mice. Branch bark extract has the ability to regulate the expression of glycometabolism genes in diabetic mice. Blood glucose levels are reduced by a Mori Cortex Radicis (MCR) ethanol-insoluble extract. MFP causes a decrease in serum and liver TG, TCH, serum LDL cholesterol, a decrease in the atherogenic index, and an increase in the levels of serum HDL cholesterol in high-fat diet-eating rats [15]. It was found that diabetic rats fed two distinct ratios of mulberry fruit polysaccharides (MFP50 and MFP90) for 49 days had decreased levels of triglycerides, fasting glucose, and fasting serum insulin. The trials demonstrate an increase in adiponectin levels and a decrease in fasting blood glucose, cholesterol, and triglyceride levels. As a result, we may assert that *M. alba* fruit has hypolipidemic and hypoglycemic effects [23].

#### **Anti- Cancer Activity:**

Mulberry phenolic extraction (MPE) block Akt and mTOR activation, which leads to autophagy in Hep3B cells. An experimental investigation found that mulberry increases mice's immunity against the development of colon cancer. By raising glycogen levels and lowering glucose levels, anthocyanin from *M. alba* can control the glucose metabolism of hepatocellular carcinoma cells. Mulberry anthocyanin inhibits the progression of stomach cancer. The expression of Beclin1 and Caspase-8 is increased by changing the ratio of LC3-II/LC3-I and BAX/BCL-2 in gastric cancer SGC-7901 cells. The Ras/PI3K signaling pathway-related melanoma metastasis is inhibited by *M. alba* anthocyanin. The *M. alba* anthocyanin inhibits the cell cycle in the S phase, preventing the tumor cells from going through additional rounds of mitosis. DNA synthesis is impeded by this. Mulberry anthocyanins trigger autophagic cell death and apoptosis. Therefore, they can be used for the treatment of cancer. *M. alba* anthocyanin shows anticancer and anti-tumor properties depending on the concentration [24]. animal tumour models are studied to observe the effect of *M. alba* polyphenols on cell separation, expansion, and apoptosis. The anti-carcinogenesis mechanisms involve antioxidant action, initiation of apoptosis, antiproliferation, detoxification and antiangiogenic movement. For example, the antiproliferation effect of aged Korean mulberries on human gastric carcinoma cells. Hydroxycinnamic acid derivatives extracted from *M. alba* fruit promotes ROS production by acting as pro-oxidants which destroys the malignant growth cells. Anthocyanins, the cyanidin 3-rutinoside, and cyanidin 3-glucoside are present in *M. alba* fruit, and they have a suppressive effect on a human lung cancer cell's invasion and movement [25].

#### **Hypolipidemic:**

Diet high in fat Lower levels of blood and liver triglycerides, total cholesterol, and serum LDL cholesterol were seen in the

bodies of rats treated with 5% or 10% mulberry fruit powder. High-density lipoprotein (HDL) cholesterol levels in the serum increased as well. Dietary fibre included in *M. alba* fruit reduces hepatic lipogenesis and increases LDL-receptor action. Mulberry fruits have a hypolipidemic impact because they are high in dietary fibre and linoleic acid. In a research, 45 g of freeze-dried *M. alba* fruit (325 mg anthocyanins) was fed to 58 hypercholesterolemic adults between the ages of 30 and 60. After 6 weeks, there was a drop in both total cholesterol and LDL (both p-values 0.001) levels. Different phytochemicals, including chlorogenic acid (CA), rutin (RT), quercetin-3-O-(6-Omalonyl)-b-D-glucoside, isoquercitrin, astragaloside, and kaempferol-3-O-(6-Omalonyl)-b-D-glucoside, are derived from various mulberry tree parts, including the fruits and leaves. These chemicals' structures are examined using mass spectrometry, NMR, UV/visible spectrophotometer, and FT infrared spectroscopy. They have phenolic properties. Based on the variability of their cultivated environments, *M. alba* plants exhibit varying polyphenol concentrations [26].

#### **Anti-Inflammatory Activity:**

A form of flavonoid extracted from mulberries is called morin. It manifests anti-inflammatory properties. On the placement of CsA in lymphatic and non-lymphoid organs as well as immune cells in mice, morin's effect was seen. CsA levels in tissues decrease as a result of morin. The mulberry bark flavonoids have anti-inflammatory properties [27]. Human endothelial cells that have been triggered by resistin are protected by the natural antioxidant curcumin and a mulberry leaf extract, as shown by real-time PCR and western blot experiments [3].

#### **Immuno-Modulatory Effect:**

The leaves and fruits of *Morus alba* exhibit immunomodulatory effects. In an experimental study, Swiss albino mice was orally administered with methanol

mulberry leaves extract, this boosted serum immunoglobulin concentration and averted mortality which was caused by bovine *Pasteurella multocida* [28]. Additionally, it increases the phagocytes score in the carbon clearing test, and the indirect haemagulation test showed circulating antibody titer as having a favorable effect on humoral and cell-mediated immunity. It was shown that the presence of polysaccharides in mulberry fruits promotes dendritic cells to phenotypically mature. As a result, it can be added to dendritic-cell tumor immunotherapy [29].

#### **Neuroprotective Activity:**

According to research on animal models of vascular dementia, *M. alba* fruit is an excellent natural neuroprotectant and cognition enhancer. The *M. alba* fruit's cyanidin-3-O-D-glucopyranoside prevents neuronal cell injury [17]. Fruit extracts from *M. alba* have neuroprotective effects. They prevent PC12 cells from suffering from oxygenation glycogen depletion (OGD), which results in cerebral ischemia damage. *M. alba* leaves undergo anaerobic processing that produces  $\gamma$ -aminobutyric acid, which increases the neuro-protective action against in vivo cerebral ischemia. It is observed that mulberry boosts the vascular reactivity of diabetic rats, this reduces oxidative stress [10].

#### **Improves postmenopausal metabolic syndrome:**

A woman faces a number of postmenopausal endocrine metabolic syndrome such as hyperglycemia, dyslipidemia, hypertension etc. Encapsulated mulberry fruit extract improves metabolic syndrome during postmenopausal period which was also proved after several experimentations in female wistar rats. The extract enhanced oxidative stress status, protein expression of tumor necrosis factor and the nuclear factor- $\kappa$ B glucose intolerance, obesity measure, cholesterol levels, atherogenic index, ACE, and weight gain [30].

#### **Conclusion:**

This review summarizes the phytochemical and pharmaceutical properties of mulberry plant. Nowadays, there is an increasing need for plant-based medicines from organic sources that have no chemicals and have lesser aftereffects. Many researches on mulberry have been done which shows the medicinal worth of this plant. It is rich in flavonoids and other bio-active compounds such as alkaloids, anthocyanins, phenolic acid etc. which exhibits antimicrobial properties and FRS effect. In conventional treatments, mulberry is utilized because it has anti-ulcer properties, immuno-modulatory, anti-oxidant, anti-cancer, anti-bacterial, anti-diabetic, hypolipidemic, anti-inflammatory, anti-hyperglycemic, anti-obesity and neuroprotective. This plant has wide scope in future for researchers to carry out study for isolation of bio-active constituents and clinical trials.

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