

# PHYTOPHARMACOLOGICAL ACTIVITY OF *MORUS ALBA* LINN. EXTRACTS – A REVIEW

Shail Bala Sanghi\* and Sabira Mushtaq

Govt. M. L. B. Girls. P. G (Auto.) College Bhopal (M.P.)

\*Corresponding Author's E mail: [shailsanghi@gmail.com](mailto:shailsanghi@gmail.com)

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## ABSTRACT

*Morus alba* Linn belongs to family Moraceae, a popular medicinal plant, has long been used commonly in Ayurvedic and many of traditional systems of medicine in Asian countries. The present paper gives an account of updated information on its phytochemicals and pharmacological activities. Currently, increasing health concern urged the researchers to revive the natural products and to fight the diseases without harming the body. In spite of medicinal uses of natural products, health supplements from natural products and their use in diet are gaining importance. The review reveals the wide range of important Pharmacological activities including antidiabetic, antimicrobial, antimutagenic, antioxidant, anticancer, anxiolytic, anthelmintic, antistress, immunomodulatory, hypocholesterolemic, nephroprotective, hepatoprotective. The plant is a very good source of ascorbic acid, of which over 90% is present in a reduced form, and also contains carotene, vitamin b1, folic acid, folinic acid, isoquercetin, quercetin, tannins, flavonoids and saponins. These reports are very encouraging and indicate that herb should be studied more extensively for its therapeutic benefits.

**Keywords:** *Morus alba*, White mulberry, Moraceae, Pharmacological review, Phytochemical review

## INTRODUCTION

*Morus alba* Linn commonly known as white mulberry belongs to family Moraceae is also known as Tut in India. *Morus alba* is a moderately sized tree, three to six meters high. White mulberry is cultivated throughout the world, wherever silkworms are raised. The leaves of white mulberry are the main food source for the silkworms.

In European countries it is grown for fruit production and it is also used as vegetable in different parts of the World, while in Japan mulberry leaves are used as tea and powder juice.<sup>1-3</sup>

It is reported that in Chinese medicine white mulberry has been widely used in medicine since 659 A.D and Chinese pharmacopoeia lists the root bark, stem, fruits and leaves as a constituent in medicinal preparations.<sup>4</sup>

Different plants have been reported for their biological activities such as anthelmintic, anti-parasitic<sup>5,6</sup> and anti-diarrheal properties.<sup>7</sup> Because of its good therapeutic activity and low toxicity *M. alba* has been extensively used in conventional Chinese medicine<sup>8</sup>. *M. alba* is reported to have neuroprotective, skin

tonic, antioxidant, anti-hyperglycemic, antibacterial, antihypertensive, and anti-hyperlipidemic activities.<sup>9,10,11</sup>

Both the leaves and the fruits can be found in many food products. Fresh white mulberry leaves for tea are processed by blanching and not blanching. In the first case tea color is green and the other black. Mulberry tea leaves have strong antioxidant properties.<sup>12</sup>

Srivastava *et al.*, (2006)<sup>13</sup> have developed a mixture consisting of lyophilized white mulberry leaves and wheat flour used for baking "paratha" - flatbread Indian popular throughout the Indian subcontinent and other Asian countries.



**Fig. 1: Fruit**



**Fig. 2: Leaves**



**Fig. 3: Whole Plant**

## **SCIENTIFIC CLASSIFICATION**

Kingdom : Plantae

Subkingdom : Tracheobionta

Super division : Spermatophyta

Division : Magnoliophyta

Class : Magnoliopsida

Subclass : Hamamelididae

Family : Moraceae

Genus : *Morus* L.

Species : *Morus alba* L.

## NUTRITIONAL ASSESSMENT

Carbohydrates, proteins, fibers, fats, minerals, vitamins and their precursors are present in significant amount.<sup>10</sup> Ercisli and Orhan (2007)<sup>2</sup> studied the chemical composition of *M. alba* fruits and reported that the weight of the fruit is 3.49 gram approximately and contains about 71.5 % moisture. *M. alba* have lower moisture contents and more fat contents (1.10%) than other species. Behenic acid (C22:0) and palmitoleic acid (C16:1) were present only in *M. alba* fruits (0.26% and 0.67%, respectively). *M. alba* has highest ascorbic acid contents (22.4 mg/100). Similar study was conducted by Srivastava et al. (2006) to estimate the nutritional composition of mulberry leaves of six genotypes. This study reported that the fresh leaves contain moisture from 71.13 to 76.68%, protein from 4.72 to 9.96%, fat from 0.64 to 1.51% and carbohydrates from 8.01 to 13.42%. While in dried mulberry leaves the moisture content decreases and it ranged from 5.11 to 7.24%, from 15.31 to 30.91% for protein, from 2.09 to 4.93% for fat and from 9.70 to 29.64% for carbohydrates. Ascorbic acid was ranged from 160 to 280 mg/100 g in fresh mulberry leaves while in dried leaves its quantity decreased and ranged from 100 to 200 mg/100 g. Similarly, in fresh leaves  $\beta$ -carotene was found to range from 10.00 to 14.688 mg/100 g, while in dried leaf powder its amount also ranged from 8.438 to 13.125 mg/100 g. The minerals content also varies in fresh and dried leaves and their composition is summarized in Table 1.

**Table 1: Mineral contents in dried and fresh *Morus alba* leaves**<sup>13</sup>

Contents in dried	<i>Morus alba</i> L. leaves	Contents in fresh <i>Morus alba</i> L. leaves
Iron (mg/100)	19.00-35.72	4.70-10.36
Zinc (mg/100)	0.72-3.65	0.22-1.12
Calcium (mg/100)	786.66-2226.66	380-786

## PHYTOCHEMISTRY OF *M. ALBA*

<sup>17</sup>

*M. alba* leaves have antioxidant components, which includes rutin, isoquercitrin, astragaloside and quercetin-3-(6-malonyl) glucoside among which quercetin - 3-(6-malonyl) glucoside is most abundant in dried mulberry leaf extract.<sup>14</sup> *M. alba* extracts have 13 known compounds. Koshihara et al. (1984)<sup>15</sup> studied the selective inhibitory effect of caffeic acid on leukotriene biosynthesis and concluded that *M. alba* has high amount of caffeic acid, which selectively inhibits leukotriene biosynthesis, that appreciably play a vital role in various diseases like asthma, allergic reactions and inflammation. The selection of the extraction solvent is very critical stage in order to extract the maximum quantity of active constituents because antioxidant components have varying polarities. Most efficient solution for the extraction of polyphenolic compound is 40% and 80% aqueous solution of ethanol and methanol. But the most suitable extraction

solvent for total phenolic contents extraction in hazelnuts is 80% ethanol solution.<sup>16</sup> Thabti et al. (2012)<sup>17</sup> determined three more compounds in mulberry leaves which are quercetin 3-O- $\beta$ -glucopyranoside-7-O- $\alpha$ -rhamnopyranoside, kaempferol-7-O-glucoside and quercetin-3-O-rhamnopyranoside-7-O-glucopyranoside. This study concluded that mulberry leaves are richest source of phytochemicals, which are beneficial for the health and can be used as vegetable. Complete range of polyphenolic compounds quantitatively determined is listed below in Table 2.

**Table 2: Quantitative analysis of polyphenolic compounds present in *M. alba***

Compound	Amount (mg/100 g)
1) 1-Caffeoylquinnic acid	58.42 - 58.90
2) Caffeic acid	1579.77 - 1588.25
3) 5-Caffeoylquinnic acid	1380.80 - 1382.28
4) 4-Caffeoylquinnic acid	124.61 - 124.93
5) Quercetin-3-O-rhamnoside -7-O-glucoside	272.60 - 273.06
6) Quercetin-3,7-D-O- $\beta$ -D-glucopyranoside	137.949 - 137.991
7) Kaempferol-7-O-glucoside	211.432 - 211.488
8) Rutin	193.69 - 194.77
9) Quercetin-3-O-glucoside	972.466 - 972.494
10) Quercetin-3-O-(6-malonyl)- $\beta$ -D-glucopyranoside	1258.58-1258.84
11) Quercetin-3-O-glucoside-7-O-rhamnoside	849.06 - 849.30
12) Kaempferol-3-Oglucopyranosyl-(1,6)- $\beta$ -Dglucopyranoside	615.98 - 616.66
13) Kaempferol-3-O-(6-malonyl)glucoside	1332.91 - 1333.75
Total phenolic acids	3148.966 - 3148.994
Total flavonols	5846.30 - 5846.72
<b>Total</b>	<b>8995.426 - 8995.546</b>

## PHARMACOLOGICAL EFFECT OF *M. ALBA*

### **Anthelmintic Effect of *M. alba***

Petroleum ether, chloroform and methanol sequential leaf extracts of *Morus alba* at Different concentrations were tested for anthelmintic capacity by the determination of time of paralysis and death of Indian earthworms, *Pheretima posthuma*. Albendazole was used as the standard all the extracts showed dose dependent effects and comparable to standard drug Albendazole.<sup>18</sup>

In a study alcoholic, petroleum ether and aqueous extract of leaves of *Morus alba* Linn were tested for anthelmintic activity. Various concentrations of alcoholic, petroleum ether and aqueous extracts were evaluated involving determination of time of paralysis and time of death of the worms. The results of present study indicated that the alcoholic, petroleum ether and aqueous extract significantly exhibited paralysis also caused death of worms especially at higher concentration of 50 mg/ml, as compared to standard drug.<sup>19</sup>

### **Antimicrobial Activity of *M. alba***

Heat Stable Proteins of *Morus alba* tested for the antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* and compared with the antibiotic chloramphenicol, Area of zone of inhibition increased with the increase in the concentration of the Heat Stable Proteins for all the microbes tested by the mulberry varieties. For *Escherichia coli* MIC was at 25 µl by *Morus alba* was more effective against *E. coli* at 100µl.<sup>20</sup>

In an another study petroleum ether, chloroform and methanol sequential leaf extracts of *Morus alba* at Different concentrations of the extracts were tested for antimicrobial activity against various bacterial strains and fungal strains. The zone of inhibition was determined against the microorganisms. The effects of these extracts were compared to standard drugs, Results of the antimicrobial activity revealed that all the extracts showed noticeable anti microbial activity in dose dependant manner against the organisms studied.<sup>18</sup>

### **Anti-stress Effect of *M. alba***

Supplementation with different nutrients and herbal preparations has been studied for adaptogenic activity during exposure to stressful conditions.<sup>21</sup> *M. alba* is one of them and in Indian traditional medicine it is used as nervine tonic.<sup>22</sup> The activity of orally administered *M. alba* fruit extracts was evaluated during and after the physical exercise in rat and change in monoamine oxidase (MAO) activities was determined. The study concluded that *M. alba* adjust the MAO activities during exercise and promote the capability

of physical activities and showed considerable anti-stress activity and enhanced the potential of physical activities. Sattayasai et al. (2008)<sup>23</sup> observed the effects of an aqueous extract of *M. alba* leaves green tea on mouse depression, anxiety, climbing activity and thermal response were evaluated. Rats were injected intraperitoneally *M. alba* leaves green tea. After 30 min of injection rats were tested in experimental models. Finally the results suggests that *M. alba* leaves green tea showed an antidepressant activity and does not show anxiolytic effect and at high doses the extract showed sedative activity to some extent. Nade et al. (2009)<sup>24</sup> studied the adaptogenic potential of ethyl acetate-soluble fraction of methanol extract of *M. alba* roots in rats. Ethyl acetate soluble fraction of methanol extract of *M. alba* roots were administered before unpredictable foot shock for 21 days. The result of the study suggested that ethyl acetate soluble fraction of methanol extract of *M. alba* roots showed significant antistress potential. Similarly, Nade and Yadav (2010)<sup>25</sup> designed a research to evaluate the anti-stress activity of *M. alba* in rats. Chronic stress was induced by restraining the rats inside a cylindrical plastic tube for 3 h daily for 10 days. The soluble fraction of *M. alba* made up of ethyl acetate at different doses were administered before production of stress. Chronic restraint stress causes cognitive dysfunction, distorted behavioral parameters, enhanced leucocytes count, superoxide dismutase (SOD), lipid peroxidation (LPO), glucose and corticosterone levels, with concomitant decrease in catalase (CAT) and glutathione reductase (GSH) activities. These observations suggested that *M. alba* have significant potential as an anti-stress agent and this study indicates that it can be used for the management of disorders induced by oxidative stress. By further exploration *M. alba* can be used as drugs alternative to conventional therapy and also health promoting supplement for the management of stress, dementia, depression and Parkinson's disease.

#### **Anti-atherogenic Activity of *M. alba***

Atherosclerosis is caused by the increased production of free radicals by endothelial and vascular smooth muscles. Free radicals through various enzyme systems initiate the process of atherogenesis. Increase in the level of low density lipoprotein cholesterol (LDL-C) or more specifically hypercholesterolemia increases the free radical production and as a result elevates lipid peroxides.<sup>26</sup> Serum cholesterol level was inhibited by butanol extract of *M. alba* leaves, which prevent atherosclerosis.<sup>27</sup> Dietary use of *M. alba* leaves and their constituents was evaluated on the progress of atherosclerotic lesions in mice. The result suggested that atherosclerotic lesions were significantly decreased as compared with that of control groups.<sup>28</sup> Similarly in hypercholesterolemic rats, the root barks 70% alcohol extract of *M. alba* inhibited the LDL induced atherogenic changes, LDL retention, oxidation, aggregation and production of lipid peroxides.<sup>29</sup> Chen et al. (2005)<sup>30</sup> studied that by feeding rabbits with *M. alba* water extract significantly reduced atherosclerosis in aorta and it was also revealed by histopathological studies.

### **Antioxidant Activity of *M. alba***

The antioxidant activity of leaf extracts was evaluated by measuring 1,1-diphenyl-2-picrylhydrazyl (DPPH•) radical scavenging activity, 2,2'-azino-bis-(3-ethylbenzthiazoline-6-sulphonic acid (ABTS•+) radical cation scavenging capacity and ferric ion reducing power and values ranged between 1.89–2.12, 6.12–9.89 and 0.56–0.97 mM Trolox equivalent/g of dried leaves, respectively. The investigated features reveal good antioxidant attributes significantly.<sup>31</sup>

In another study radical scavenging activity of different parts of mulberry (*Morus alba* L.) were determined. Methanol extracts and their fractions dose dependently increased radical scavenging activity of mulberry branches, roots and leaves (more than 70%). Study shows that mulberry fruits exhibited the highest radical scavenging activity.<sup>32</sup>

### **Anti- Cancer Activity of *M.alba***

Cancer is one of the major causes of death in animals specially felines and canines. It was observed that longer the life of animals, the chance of exposure to carcinogenic agents increased. Because of high incidence of cancer, new studies are currently being performed with the aim of finding better and safer therapeutic agents.<sup>33</sup> Prenylated flavanone, 7, 2', 4', 6'-tetrahydroxy-6geranylflavanone separated from ethyl acetate extracts of *M. alba* root showed cytotoxic activity against hepatoma cells in rats with an IC50 of 52.8 mg/mL.<sup>34</sup> Similarly, 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.<sup>35,36</sup> Methanolic extract obtained from *M. alba* and its sub fractions obtained from aqueous, butanol and chloroform fractions blocked or inhibited the NO production and significantly reduced the formation of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) in macrophages, which were LPS activated RAW2647.<sup>37</sup> Further evaluation and clinical trials may reveal the therapeutic potential of *M. alba* against cytotoxic cells, which may help in finding a cheap and easily available source for treatment of cancer and decreasing invasiveness of cancerous cells.

## **DISCUSSION**

It is truth that without nature human life is not possible. The food, clothes and shelter are three basic necessity of human beings and an important one necessity is good health, which provided by plant kingdom.<sup>38</sup> In spite of the overwhelming influences and our dependence on modern medicines and tremendous advances in synthetic drugs, a large segment of the world population still likes drugs of plants origin. Of the 2,50,000 higher plant species on earth, more than 80,000 are medicinal. However, only 7000-7500 species are used for their medicinal values by traditional communities.<sup>39</sup> Now a days *Morus*

*alba* has been investigated in various scientific instigations in order to explore its active constituents, which may have medicinal value. It is a rich source of flavonoids and other compounds which showed antimicrobial potential and free radical scavenging activity. *M. alba* is used in traditional medicine and claimed to have kidney tonic, liver tonic, cardio-protective, skin whitening, anti-hyperglycemic, neuroprotective and anti-ulcer activities. The main use of this medicinal plant is antidiabetic, immunomodulatory, antimicrobial, antioxidant and anticancer. It is on the precise notes that this review will pay special attention toward the therapeutical capabilities, uses and in vast studies of Phytochemical and Pharmacological features of *Morus alba*.

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