Comprehensive Notes on Phytochemical and Pharmacological Activity of *Morus alba*

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Abstract

Herbal medicine has minimum side effect and treat the diseases from root level. Presently global pharmaceutical market has good response for herbal medicines, herbal cosmetics and nutraceuticals. The pharmacological activity of medicinal plants is due to presence of secondary metabolite namely alkaloids, glycosides, flavonoids, steroids, tannins, polyphenol etc. The herbal medicines are used for the treatment of cancer, diabetes, hypertension, cardiovascular diseases, inflammation, fever, skin diseases etc. *Morus alba* belongs to family Moraceae has potent pharmacological activity and prescribed for the ailment of different diseases. The different parts of *Morus alba* are worthy source of active constituents namely Albanol, Albafuran, Kuwanol, Murasin, Hydroximorasin and Moranoline, phytosterols, triterpenes, sitosterols, benzofuran derivatives, morusimic acid, anthraquinones, glycosides, oleanolic acid, anthocyanins etc. The present review paper illustrate the scientifically reported phytochemical and pharmacological activity of *Morus alba*. The researchers working on herbal medicines get all the comprehensive updates related to phytochemical and pharmacological activity of *Morus alba* from this study.

1 Introduction

Medicinal herbs have been known to be an important potential source of therapeutics aids. Medicinal plants not only uses for the treatment of diseases but also as potential material for maintaining good health and conditions¹. Medicinal plants may be defined as those plants that are commonly used in treating and preventing specific ailments and diseases and that are generally considered to be harmful to humans. Two-third of the world's population depends on herbal medicine for primary health care. The reasons for this is because of their better cultural acceptability, better compatibility and adaptability with the human body and pose lesser side effects. Medicinal plants contain a wide variety of secondary metabolites or compounds such as tannins terpenoids, alkaloids, flavonoids; that dictates the therapeutic potency of the plants most especially the antimicrobial activities. Among the plant species used for medicinal purposes are those of the genus *Morus*. The most known species are *Morus alba*, *rubra*, and *nigra*.

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. Mulberry is exclusively used for rearing silkworm due to the presence of unique chemo-factors like morin, β -sitosterol in leaves.

Mulberry is a native to Pakistan, India and Nepal, east-wards to Myanmar, Indochina, China and Japan. It is extensively cultivated throughout the plains of India and Pakistan, and in the Himalayan hills up to 3,300 m elevation. It is also cultivated in Europe and throughout most of Asia, and is occasionally naturalized^{2,3}.

2 Phytochemical

The plant is a very good source of folic acid, carotene, vitamins, flavonoids, tannins, saponins, ascorbic acid and antioxidants, bioflavonoids, moracetin, rutin, isoquercetin and quercetin-3-

triglucoside, sterols, β -Sitosterol, amino acid and organic acid, triterpenes, volatile oil, alkaloids, 1-deoxynojirimycin, prostaglandin E2, nitric acid and cytokinin, calystegin, Albanol, Albafuran, Kuwanol, Murasin, Hydroxymorasin and Moranoline, phytosterols, triterpenes, sitosterols, benzofuran derivatives, morusimic acid, anthraquinones, glycosides, oleanolic acid and anthocyanins⁴.

Leaf contains triterpenes (lupeol) Sterols (β - Sitosterol), bioflavonoids (rutin, moracetin, quercetin-3-triglucoside, apigenin and isoquercitrin), 1-deoxynojirimycin, coumarins, volatile oil, alkaloids, amino acids and organic acids as bioactive constituents. *Morus alba* leaf extract has been found to produce nitric acid, prostaglandin E2 and cytokines in macrophages^{5, 6}. Plants inhibit peroxidation due to the presence of a high amount of linoleic acid, α -tocopherol or vitamin E (approx. 72%). On the other hand, the presence of anthocyanin which is a hydrophilic pigment is directly proportional to its antioxidant activity⁷.

Many flavones, polysaccharide were isolated from the root bark such as Moranoline, Albafuran, Albanol, Morusin, Kuwanol, Calystegin and Hydroxymorcin.

The plant is reported to contain the phytoconstituents tannins, phytosterols, sitosterols, saponins, triterpenes, flavonoids, benzofuran derivatives, morusimic acid, anthocyanins, anthroquinones, glycosides and oleanolic acid as the main active principles⁸⁻¹¹.

3 Pharmacological Activity

3.1 Antidiabetic activity

Ethanol extract of *Morus alba* root barks reduced the amount of the glucose, increased insulin production, protected pancreatic β cells from degeneration, diminished lipid peroxidation, inhibited low density lipoprotein (LDL) atherogenic modification and lipid peroxides formation, and increased the expression of adipogenic maker proteins, such as peroxisome proliferator-activated receptors γ (PPAR γ), adipocyte-specific fatty acid binding protein 4 (aP2), and GLUT4 (glucose transporter 4)¹²⁻¹⁴.

Methanolic extract of *Morus alba* was tested for its in-vitro acetylcholine esterase inhibitory activity using modified Ellmann's method. The crude methanolic extract showed acetylcholine esterase inhibitory activity in a concentration dependent manner and around 10 μ g of the extract was required for 50% inhibition of the activity¹⁵.

The animals were treated with mulberry leaf extract at different doses for 35 days. The various parameters studied included blood glucose. According to the histological and biochemical results it was concluded that the extract of this plant may reduce blood glucose levels by regeneration of β cells¹⁶.

3.2 Antistress activity

The ethyl acetate-soluble fraction of methanol extract of *Morus alba* roots was subjected to evaluate the adaptogenic property against a rat model of chronic stress (CS). The anti-stress efficacy was tested by determining the behavioral and biochemical parameters such as open field, cognitive dysfunction, leucocytes count, blood glucose and corticosteroid levels. Pre-treatments with the ethyl acetate soluble fraction of methanol extract of *Morus alba* roots (25, 50 and 100 mg/kg, p.o.) significantly attenuated the CS-induced perturbations. The results indicated that *Morus alba* possesses significant adaptogenic activity, indicating its possible clinical utility as an antistress agent¹⁷.

3.3 Anthelmintic activity

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 (petroleum ether, chloroform and methanol) showed dose dependent effects and comparable to standard drug Albendazole¹⁸.

In a study alcoholic, petroleum ether and aqueous extract of leaves of *Morus alba* Linn were tested for anthelmintic activity, involving determination of time of paralysis and time of death of the worms. The results 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 drug¹⁹.

3.4 Antimicrobial activity

Different concentrations of leaf extracts of *Morus alba* (petroleum ether, chloroform and methanol) 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 studied¹⁸.

Crude extracts of *Morus alba* have been tested for antibacterial and antifungal activities. The analysis of structure-activity relationship revealed that most of the bioactive compounds such as flavonoids and terpenoids exhibit potent antimicrobial activity. The arylbenzofurans isolated from *Morus* species including Moracin C and Moracin M showed promising antimicrobial activity against methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Prenylated compounds also showed antifungal activity at the concentration range of (6.25–120.00) μ g/mL and antibacterial activity at a dose range of (6.25–100.00) μ g/mL. The higher antimicrobial activity of the prenylated flavonoids is due to their hydrophobic nature which makes them capable to easily penetrate through the microorganism cell membrane²⁰.

3.5 Anti-dopaminergic effect

The methanolic extract of *Morus alba* leaves was evaluated on haloperidol and metoclopramide induced catalepsy, foot shock-induced aggression, amphetamine-induced stereotyped behavior and phenobarbitone induced sleeping in mice. The inhibitory effect of the extract on dopamine was studied using isolated rat vas deferens. In each of these tests, the extract was administered in doses of 50, 100 and 200 mg/kg, *i.p.*, 30 min before performing the test in mice. The extract significantly reduced number of fights and increased latency to fights in foot shock-induced aggression; it also decreased amphetamine induced stereotyped behavior in a dose dependent manner. The sleeping time induced by phenobarbitone too was prolonged. The extract inhibited contractions produced by dopamine on isolated rat vas deferens. The results suggested that the leaves of *Morus alba* may have potential clinical application in the management of psychiatric disorders²¹.

3.6 Antimutagenic activity

Studies showed that the mixture of *M. alba* and *M. nigra* possess genoprotective properties on the structure and functions of plants and animals cells. These extracts may diminish the mutation level caused by the chemical mutagens such as X-rays and gamma rays²².

3.7 Antioxidant activity

Morus alba root bark showed strong free radical scavenging effect and inhibitory effect of xanthine oxidase and lipid peroxidation²³.

Water extract of *Morus alba* root bark showed antioxidant effects in assays FeCl₂–ascorbic acid-induced lipid peroxidation in rats²⁴

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 activity²⁵.

Methanolic extract showed antioxidant activity through ameliorating the level of blood glutathione content, superoxide dismutase, and catalase activities²⁶.

The antioxidant activity of leaf extracts was evaluated by measuring 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 significantly²⁷.

3.8 Anticancer activity

Methanol extracts of mulberry leaves has also shown promising anti-proliferative and anticancer efficacy on various cancer cells lines including Calu-6 (human pulmonary carcinoma), breast cancer cells (MCF-7), HCT-116, human gastric carcinoma (SNU-

601) cell line. It was observed that the anti-proliferative activity of methanol extract of mulberry leaves could be enhanced by the fermentation process only against human gastric carcinoma (SNU-601) cell line in concentration of 1 000 mg/mL²⁵.

Morus alba root extract also exhibited cytotoxic activity on human leukemia cells (K-562, B380) and mouse melanoma cells (B16) by inhibiting microtubule assembly and induced cell growth arrest and apoptosis in human colorectal cancer cells (SW480) by activating ATF3 expression and down-regulated cyclin D1 level²⁸.

3.9 Immunomodulatory activity

The immunomodulatory effects of *M. alba* was evaluated by using different experimental models such as effect on serum immunoglobulins, cyclophosphamide induced neutropenia, carbon clearance test, neutrophil adhesion test, mice lethality test and indirect haemagglutination test. Results showed that the administration of *M. alba* in mice tend to increase serum immunoglobulins levels and prevent the mortality induced by bovine *Pasteurella multocida* in mice. It also significantly reduced neutropenia and significant increased the phagocytic index in carbon clearance assay²⁹.

Aqueous leaf extract of *Morus alba* was tested for hypersensitivity and haemagglutination reaction using sheep red blood cells as the antigen. The *Morus alba* offers an increase in delayed type hypersensitivity reaction and the effect is comparable with that of the standard drug levamisole. *Morus alba* however facilitates a considerable increase in total leukocyte, lymphocyte, neutrophil and eosinophil count doses dependently. *Morus alba* was found to induce a better immunomodulatory activity³⁰.

3.10 Hypocholesterolemic activity

The 70% alcohol extract of the *Morus alba* root bark was fractionated with water, 50% methanol and finally with 100% methanol. Experimentally induced atherosclerosis was produced by feeding rats a diet enriched in coconut oil (25% by weight) and cholesterol (2% by weight) for 21 days. Then extracts were orally administered to hypercholesterolemic rats in different doses for 15 successive days, in order to evaluate their expected hypocholesterolemic activity. The results revealed that extract may act as potent hypocholesterolemic nutrient¹².

3.11 Nephroprotective activity

The nephroprotective effect of hydroalcoholic extract and flavonoid fraction of *Morus alba* leaves on cisplatin-induced nephrotoxicity in male rats was investigated. Hydroalcoholic extract was ineffective in reversing the alterations but flavonoid fraction significantly inhibited CP-induced increases of blood urea nitrogen and creatinine. Flavonoid fraction could also prevent CP-induced pathological damage of the kidney. The flavonoid fraction of *Morus alba* can protect kidneys from CP-induced nephrotoxicity³¹.

3.12 Hepatoprotective effect

The crude hydroalcoholic extract of *Morus alba* leaves was evaluated for hepatoprotection against hepatotoxicity induced by carbon tetrachloride. The hydroalcoholic extract at dose of 800mg/kg exhibited a significant liver protective effect by lowering the serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT), decreasing the sleeping time and resulting in less pronounced destruction of the liver, there was no fibrosis and inflammation³².

Further more Carbon tetrachloride produced significant changes in biochemical parameters (increases in serum glutamate pyruvate transaminase (SGPT), Serum glutamate oxaloacetate transaminase (SGOT), alanine phosphatase (ALP) and serum bilirubin.) and histological (damage to hepatocytes) using Standard drug Liv-52. Pretreatment with alcoholic extract and water extracts significantly prevented the biochemical and histological changes induced by CCl₄ in the liver. The study showed that the alcoholic extract and water extracts of mulberry possessed hepatoprotective activity³³.

3.13 Anti-HIV activity

From *Morus alba* fourteen different type of compounds were isolated and then tested against HIV. The results showed that the ethanolic extract of *Morus alba* contains different kind of compounds like mulberrofuran D, mulberrofuran G, mulberrofuran K, kwanon G, kwanon H, morusin and their derivatives. Morusin, kuwanon H, morusin and morusin 4-glucoside revealed HIV activity¹¹.

3.14 Antiallergic activity

The strong antihistaminic and antiallergic activity showed by the extract obtained from the root bark of *Morus alba* in hot water. The most widely and extensively studied species is *Morus alba* that has been reported to have antiallergic activity³⁴.

3.15 Gut and airways disorders

Crude extract of *Morus alba* at 100 mg/kg exhibited protective effect against castor oil-induced diarrhea in mice. It caused suppression of carbachol induced increase in inspiratory pressure of anaesthetized rats. In guinea-pig trachea, *Morus alba* completely inhibited low K⁺ contractions, with partial effect on high K⁺. *Morus alba* possesses a combination of KATP channel opening, weak Ca⁺⁺-antagonist and phosphodiesterase inhibitory mechanisms, which explain its medicinal use in hyperactive gut and airways disorders³⁵.

4 Traditional uses

Morus alba has been use by tribals for ailments such as asthma, cough, bronchitis, edema, insomnia, wound healing, diabetes, influenza, eye infections, urinary incontinence, tinnitus, dizziness, constipation and nosebleeds. Traditionally, the mulberry fruit has been used as a medicinal agent to nourish the

blood, benefit the kidneys and treat weakness, fatigue, anemia and premature graying of hair. The white mulberry has been used in the indigenous system of medicine for cooling, acrid, purgative, diuretic, laxative, anthelmintic, brain tonic, antibacterial, hepatopathy properties. They are useful in vitiated condition of vata and pitta, burning sensation³⁶⁻³⁸.

Chinese people used *Morus alba* from ancient time for various medicinal purposes and almost they utilized all parts of *Morus alba* as a medicine. The root barks of *Morus alba* is used as dietary Chinese herbs, it has been used in doses 9–15 g by decocting method for the treatment of cough, yellow sputum, bronchitis, xerophthalmia, nephritis, pulmonary diseases, incised wound, and so on³⁹.

5 Conclusion

The present paper illustrate the pharmacological activity, phytochemical and traditional uses of *Morus alba*. The reported pharmacological activity justify the medicinal properties of *Morus alba* claimed by traditional healers. This plant has wide scope in future for researchers to carry out study in isolation of active constituents and clinical trial.

6 Conflict of interest

None

7 Author's contributions

VD carried out literature review, while KWS draft the manuscript. Both authors read and approved the final manuscript.

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