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Review Article

MORUS ALBA LINN: A PHYTOPHARMACOLOGICAL REVIEW

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ABSTRACT

Morus alba Linn, a popular medicinal plant belongs to family Moraceae, has long been used commonly in Ayurvedic and many of traditional systems of medicine. The present paper gives an account of updated information on its Phytochemicals and Pharmacological activities. The review reveals the wide range of important Pharmacological activities including antidiabetic, antimicrobial, antimutagenic, antioxidant, anticancer, anxiolytic, anthelmintic, antistress, immunomodulatory, hypocholesterolemic, nephroprotective, hepatoprotective. Various other effects like adaptogenic effect, effect on hyperlipidemia, inhibition of melanin biosynthesis used in psychiatric disorder, also in gut and airways disorders. 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 b_1, 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,* Moraceae, Pharmacological review, Phytochemical review

INTRODUCTION

For the eternal health, longevity and remedy, to remove pain and discomfort, fragrance, flavor and food mankind all over the world dependent upon the plant kingdom to meet their all needs. Medicinal plants still play important role in emerging and developing countries. Medicinal plants are the major components of all indigenous or alternative systems of medicine. Medicinal plants are sources and can be a good start for the discovery of new chemical compound which leads to new drug[1]. *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. The plant is known by various names in different languages as: Sanskrit: Tutam; Hindi: Tut; English: Mullberry; Malayalam: Malbari; Tamil: Musukette[2].

HABIT

Shrub or tree 3.10 m tall. Bark grey, shallowly furrowed. Branches fine hairy. Winter buds reddish brown, ovoid, finely hairy. Stipules lanceolate, 2.3-5 cm, densely covered with short pubescence. Petiole 1.5-5.5 cm, pubescent; leaf blade ovate to broadly ovate, irregularly lobed, 5.30 × 5.12 cm, abaxially sparsely pubescent along midvein or in tufts in axil of midvein and primary lateral veins, adaxially bright green and glabrous, base rounded to ± cordate, margin coarsely serrate to crenate, apex acute, acuminate, or obtuse. Male catkins pendulous, 2.3-5 cm, densely white hairy. Female catkins 1.2 cm, pubescent; peduncle 5.10 mm, pubescent. Male flowers: calyx lobes pale green, broadly elliptic; filaments inflexed in bud; anthers 2-loculed, globose to reniform. Female flowers: sessile; calyx lobes ovoid, ± compressed, with marginal hairs; ovary sessile, ovoid; style absent; stigmas with mastoid like protuberance, branches divergent, papillose. Syncarp red when immature, blackish-purple, purple or greenish white when mature, ovoid, ellipsoid or cylindrical, 1.2-5 cm. Fl. Apr-May, fr. May-Aug[3].

HABITAT

Morus alba is native of India, China and Japan. It is occasionally cultivated elsewhere in Europe, North America, and Africa. *Morus alba* is commonly known as white mulberry. White mulberry is cultivated throughout the world, wherever silkworms are raised. The leaves of white mulberry are the main food source for the silkworms[2].

TAXONOMICAL CLASSIFICATION[4]:

Kingdom	:*Plantae* – Plants
Subkingdom	:*Tracheobionta* – Vascular plants
Superdivision	:*Spermatophyta* – Seed plants
Division	:*Magnoliophyta* – Flowering plants
Class	:*Magnoliopsida* – Dicotyledons
Subclass	:*Hamamelididae*
Order	:*Urticales*
Family	:*Moraceae* – Mulberry family
Genus	:*Morus* L. – mulberry
Species	:*Morus alba* L. – white mulberry

ETHNOMEDICINAL REVIEW

This widely grown plant has been in use by tribals of this country for ailments such as asthma, cough, bronchitis, edema, insomnia, wound healing, diabetes, influenza, eye infections and nosebleeds[2]. 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. It is also used to treat urinary incontinence, tinnitus, dizziness and constipation in the elderly patient[5]. The white mulberry has a long history of medicinal use in Chinese medicine; Almost all the parts of the plant are used as Medicine[6]. It 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 sensation[7].

PHYTOCHEMICAL REVIEW

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, which act as a good source of natural antioxidants[2]. White mulberry leaf contains triterpenes (lupeol) Sterols (β-Sitosterol), bioflavonoids (rutin, moracetin, quercetin-3-triglucoside and isoquercitrin), coumarins, volatile oil, alkaloids, amino acids and organic acids. *Morus alba* leaves contain rutin, quercetin and apigenin as bioactive constituents[8]. The one of major constituent of *Morus alba* is 1-deoxynojirimycin[9]. *Morus alba* leaf extract has been found to produce nitric acid, prostaglandin E2 and cytokines in macrophages. Further, a polysaccharide isolated from *Morus alba* root bark[10]. Many flavones were isolated from the root bark as active principles[11]. Many biochemical compounds such as Moranoline, Albafuran, Albanol, Morusin, Kuwanol, Calystegin and Hydroxymoricin are isolated from mulberry plants which play an important role in pharmaceutical industry[12]. Review shows the presence of thiamine, protein, carbohydrates. 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 principles[2,13,14,15].

Fig. 1: Fruit

Fig. 2: Leaves

Fig. 3: Leaves

Fig. 4: Whole Plant

Fig. 5: Stem

Fig. 6: Root Bark

PHARMACOLOGICAL REVIEW

Antidiabetic

Morus alba were studied for the starch breakdown by α-amylase in vitro *Morus alba* [IC50=17.60 (17.39-17.80) mg/ml] revealed appreciable α-amylase inhibitory activities in a concentration-dependent manner[16].

In an another study the 50% 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 µg of the extract was required for 50% inhibition of the activity[17].

In a histopathologic study the effects of *Morus alba* leaf extract on the pancreas of diabetic rats were studied. The animals were treated with mulberry leaf extract at different doses for 35 days. The various parameters studied included blood glucose, the relative body weight of the pancreas, the diameter of islets and the number of β cells in all groups. 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 cells[18].

Antistress

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). 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 indicate that *Morus alba* possesses significant adaptogenic activity, indicating its possible clinical utility as an antistress agent[19].

Anthelmintic

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[20].

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[21].

Antimicrobial

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 chlorempheniсol, 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[22].

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[20].

Anti-dopaminergic Effect:

The methanolic extract of *Morus alba* L. leaves was evaluated on haloperidol and metoclopramide induced catalepsy, foot shock-induced aggression, amphetamine-induced stereotyped behavior and phenobarbitone induced sleeping in mice. Further the inhibitory effect of the extract on dopamine was studied using isolated rat vas deferens. The extract produced significant dose dependent potentiation of haloperidol and metoclopramide induced catalepsy 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 deferensThe results suggest that the leaves of *Morus alba* L. may have potential clinical application in the management of psychiatric disorders[23].

Antimutagenic Activity

The influence of *Morus alba* and mixture with *Morus nigra* leaf extracts, on the structure and functions of plants and animals cells were studied. The absence of the genotoxicity of the extracts and their mixture has been established. All active biological compounds studied demonstrate genoprotective properties. The studied extracts and their mixtures decreased the mutability level induced with chemical mutagens, gamma-rays and ageing in the plants (*Vicia faba, Arabidopsis thaliana)* and animals (rats) cells[24].

Antioxidant Activity

The antioxidant activity of leaf extracts was evaluated by measuring 1,1-diphenyl-2-picrylhydrazyl ($DPPH^{\bullet}$) radical scavenging activity, 2,2'-azino-bis-(3- ethylbenzthiazoline-6-sulphonic acid ($ABTS^{\bullet+}$) 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[25].

In an 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[26].

Anticancer

In a study antiproliferative properties of different parts of mulberry (*Morus alba* L.) were determined. The antiproliferative effect of the methanol extracts of mulberry leaves on the cell lines Calu-6 (human pulmonary carcinoma), MCF-7 (human breast adenocarcinoma) and HCT-116 (human colon carcinoma) was different and connected to the concentrations of the investigated extracts. The fermentation of the mulberry leaves did increase their methanol extract antiproliferative effect only on human gastric carcinoma (SNU-601) cell line in concentration of 1,000 mg mL-1[26].

Anxiolytic

The anxiolytic effect of a methanolic extract of *Morus alba* L. leaves in mice was study by using the hole-board test; elevated plus-maze paradigm; open field test and light/dark paradigm were used to assess the anxiolytic activity. *Morus alba* extract at different doses and diazepam as standard were administered 30 min before the tests. The results showed that the methanolic extract of *Morus alba* significantly increased the number and duration of head poking in the hole-board test. In the elevated plus-maze, the extract significantly increased the exploration of the open arm in similar way to that of diazepam. Further, in the open field test, the extract significantly increased rearing, assisted rearing, and number of squares traversed, all of which are demonstrations of exploratory behavior. In the light/dark paradigm, the extract produced significant increase in time spent in the lighted box as compared to vehicle. The spontaneous locomotor activity count, measured using an actophotometer, was significantly decreased in animals pretreated with *Morus alba* extract, indicating a remarkable sedative effect of the plant. The results of the present study suggest that a methanolic extract of *Morus alba* leaves may possess an anxiolytic effect[27].

Gut and Airways Disorders

Crude extract of *Morus alba* at 100 mg/kg exhibited protective effect against castor oil-induced diarrhea in mice. In isolated rabbit jejunum, *Morus alba* inhibited the spontaneous contractions and caused glibenclamide-sensitive inhibition of low K^+ induced contractions, with mild effect on high K^+. Similarly, cromakalim caused inhibition of low K^+, but not of high K^+, while verapamil did not differentiate in its inhibitory effect on two concentrations of K^+. *Morus alba* 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* caused leftward shift of isoprenaline-induced inhibitory concentration response curves, like papaverine. These results indicate that *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 disorders[28].

Immunomodulatory

The effect of *Morus alba* on the immune system was evaluated by using different experimental models such as carbon clearance test, cyclophosphamide induced neutropenia, neutrophil adhesion test, effect on serum immunoglobulins, mice lethality test and indirect

haemagglutination test. *Ocimum sanctum* was used as standard drug. *Morus alba* extract indifferent doses increased the levels of serum immunoglobulin and prevented the mortality induced by bovine *Pasteurella multocida* in mice. It also increased the circulating antibody titre in indirect haemagglutination test. On the other hand, it showed significant increase in the phagocytic index in carbon clearance assay, a significant protection against cyclophosphamide induced neutropenia and increased the adhesion of neutrophils in the neutrophil adhesion test. Hence, it was concluded that *Morus alba* increases both humoral immunity and cell mediated immunity[29].

In another study aqueous leaf extract of *Morus alba* was evaluated for the immunomodulatory activity. Wistar rats were used as the specimen. The extract is 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. It does not induce any significant alterations in antibody titer value. *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 activity. It is inferred that *Morus alba* aqueous extract stimulates the innate or nonspecific immune system in a dose dependant manner and does not stimulate the adaptive immune system in mediating immunomodulatory property[30].

Hypocholesterolemic

The 70% alcohol extract of the *Morus alba* L. 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 nutrient [31].

Nephroprotective

A study was designed to investigate the nephroprotective effect of hydroalcoholic extract and flavonoid fraction of *Morus alba* leaves on cisplatin-induced nephrotoxicity in rats. Male rats were used in this study. Study involved the serum concentrations of blood urea nitrogen (BUN), creatinine (Cr) and nitric oxide testing using standard methods. Also left kidneys were prepared for pathological study. Hydroalcoholic extract was ineffective in reversing the alterations but flavonoid fraction significantly inhibited CP-induced increases of blood urea nitrogen and creatinine. None of the treatments could affect serum concentration of nitric oxide. Flavonoid fraction could also prevent CP-induced pathological damage of the kidney. It seems that concurrent use of flavonoid fraction of *Morus alba* with CP can protect kidneys from CP-induced nephrotoxicity[32].

Hepatoprotective Effect

The crude hydroalcoholic extract of *Morus alba* L. 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 inflammation.[33].

Inhibition of Melanin Biosynthesis

A study was carried out to investigate the *in vitro* effects of an 85% methanol extract of dried *Morus alba* leaves on melanin biosynthesis, which is closely related to hyperpigmentation. These extracts inhibited the tyrosinase activity that converts dopa to dopachrome in the biosynthetic process of melanin. Mulberroside F, which was obtained after the bioactivity-guided fractionation of the extracts showed inhibitory effects on tyrosinase activity and on the melanin formation of melan- a cells. This compound also exhibited superoxide scavenging activity that is involved in the protection against autooxidation. But its activity was low and was weaker than of kojic acid. These results suggest that mulberroside F isolated from mulberry leaves might be used as a skin whitening agent[34].

DISCUSSION

It is truth that without nature human being 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[35]. 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[36]. In traditional medicine, there are many natural crude drugs that have the potential to treat many disease and disorders one of them is *Morus alba* having many nutritional as well as therapeutic activities. This particular have a wide established and hidden therapeutic uses. The major use of this medicinal plant is antidiabiatic, immunomodulatory, antimicrobial, antioxidant and anticancer. It is look for the appropriation 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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