

A Review of different Phytochemicals and Pharmacological activities evaluations of *Morus alba* (L.)

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Abstract: *The rich source of medicine is plants showing various pharmacological characteristics against specific diseases since ancient times. In present days the increasing health problem and their concern attracted the biologists to search for plants and the chemicals in them to alleviate the diseases without harming the body. The major objectives of this review are to find out nutritional value, bio-elements and pharmacological activities of Morus alba. The phytochemicals isolated from the different parts viz. root, leaves and bark of Morus alba having alkaloids, flavonoids and tannins etc which exhibit biological activities viz. antibacterial, antidiabetic, antioxidant, anti-inflammatory and anti-HIV activities.*

Keywords: *Alkaloids, Antibacterial, Biological activities, Morus alba, Phytochemicals*

INTRODUCTION

Distribution

Morus alba is a native to Pakistan, Nepal and India, east-wards to China, Indochina and Japan. In plain areas Pakistan and India *Morus alba* species is extensively cultivated. In Himalayan hills in Pakistan up to 3300 meters height for its foliage which is used as a food source for silkworms. In Europe and Asia *Morus alba* is cultivated and is occasionally naturalized (Anonymous, 1952).

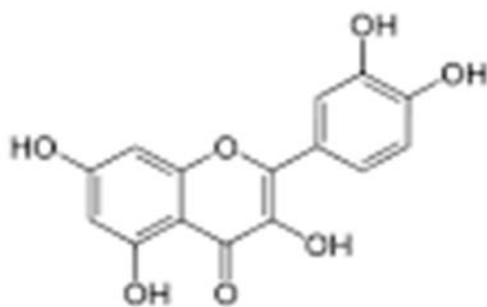
Cultivation

Morus alba trees can be propagated by grafting, cutting and seeds. Before sowing to avoid disease the seeds must be treated with camphor water. Thin layer ashes and soil spread over the seed after sowing. The beds must be kept moist. The seed will be germinated in nine to fourteen days depending upon the seasonal conditions. Seedlings are used as transplant for bush *Morus alba* and for trees when seedlings are ten to fifteen cm tall. Although *Morus alba* plants are more expensive from seedlings but it give better plants from cutting. In India root grafting is practiced usually in furrows and pits root cuttings are planted. In the month of April and May cutting are planted in furrows they will be 10 cm apart when irrigation is used the furrows being twenty two cm apart. The better root system developed by grafted plants are used specially in Japan then those developed by seedling, cutting or layering. This will be very suitable for irrigated area when

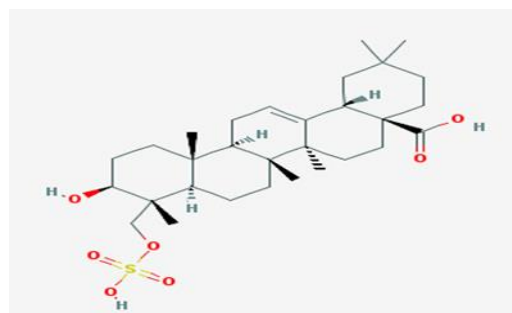
grafted trees planted 1.6meters apart from each other. To train and prune *Morus alba* plants there are some different techniques which were employed. For each pruning the field is properly manure and cultivated (Doi et al., 2001).

Chemical constituents

There are various types of chemicals present in *Morus alba* viz. folic acid, carotene, vitamins, flavonoids, tannins, saponins, ascorbic acid and antioxidants, bioflavonoids, moracetin, rutin, isoquercetin and quercetin-3-triglucoside, sterols, β -Sitosterol, aminoacid and organic acid, triterpenes, volatile oil, alkaloids, 1-deoxynojirimycin, prostaglandin E2, nitric acid and cytokinin, calystegin, Albinol, Albafuran, Kuwanol, Murasin, Hydroximorasinesand Moranoline, phytosterols, triterpenes, sitosteroles, benzofuran derivatives, morusimic acid, anthraquinones, glycosides, oleanolic acid and anthocyanins are present as a main active principles (Kim et al., 2000).

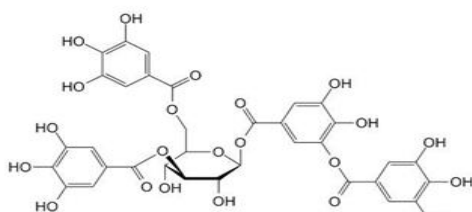


Quercetin

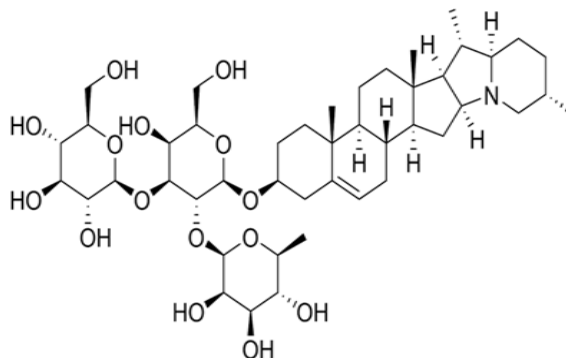


Terpene

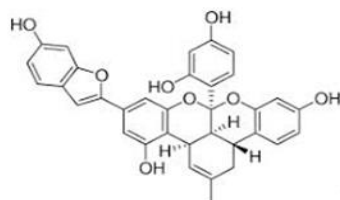
Structure of tannic acid



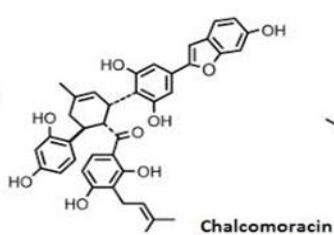
Tannin



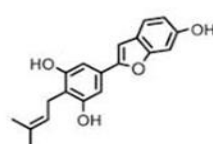
Saponin



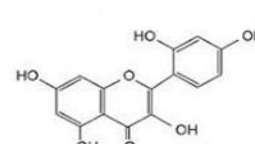
Albinol A



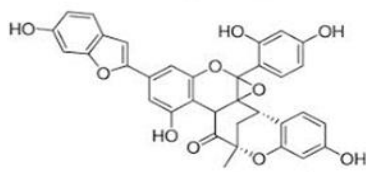
Chalconoracin



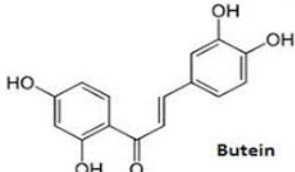
Moracin C



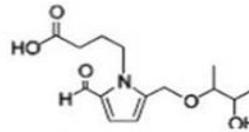
Morin



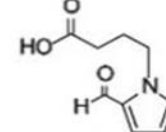
Mulberrofurane Q



Butein



Morrole A



2-formyl-1H-pyrrole-1-butanoic acid

Figure1: Structure of different chemical constituents present in *Morus alba*

Nutritional Assessment

Fats, carbohydrates, proteins, fibers, vitamins and minerals are present in *Morus alba* and their precursors are present in significant amount (Ouyang et al., 2005). The chemical composition of *Morus alba* fruits was find out by Ercisli and orhan (2007) as well as they reported that the fruits of *Morus alba* contain moisture about 71.5% and the weight of the fruit is about 3.49grams. *Morus alba* have lower moisture quantity and have more fat contents (1.10%). *Morus alba* contains palmitoleic acid, behemic acid and ascorbic acid. To find out the nutritional compositions of *Morus alba* leaves of six genotype a experiment was performed by Srivastava *et al.*, (2006) and they reported that the fresh leaves of *Morus alba* contain carbohydrate 8.01-13.42%, proteins 4.72-9.96%, fats 0.64-1.51% and contain moisture from 71.13-76.68% while the dried leaves of *Morus alba* contain carbohydrates 9.70-29.64%, proteins 15.31-30.91%, fats 2.09-4.93% and the moisture quantity decreases up to 5.11-7.24%. The quantity of ascorbic acid in fresh leaves range from 160-280mg/100g while in dried leaves this quantity decreases up to 100-200mg/100g. The quantity of β -carotene in dried leaves ranges from 8.438-13.125mg/100g while in case of fresh leaves 10.00-14.688mg/100g (Chu et al., 2006). In similar way the minerals contents are varies in dried and fresh leaves and their composition is summarized in the Table.1

Table 1. Minerals contents in dried and fresh *Morus alba* leaves

Mineral contents in dried and fresh leaves of <i>Morus alba</i>		
Minerals	Contents in dried <i>Morus alba</i> leaves	Contents in fresh <i>Morus alba</i> 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



Figure 2: Fruit



Figure 3: Stem



Figure 4: Leaves



Figure 5: Root Bark

Ethnomedicinal importance of *Morus alba*

From ancient time *Morus alba* has been in use for different ailments such as edema, insomnia, bronchitis, cough, asthma, diabetes, wound healing, eye infection, influenza and nosebleed (Bose, 1989). As a medicinal agent the fruits of *Morus alba* has been used to treat weakness, anemia, to nourish blood, fatigue, benefit the kidney, premature graying of hair as well as to treat dizziness, tinnitus, constipation in the elderly patient and urinary incontinence (Nomura et al., 1983). Chinese people used *Morus alba* from ancient time for various medicinal purposes and almost they utilized all parts of *Morus alba* as a medicine. This important plant has been used in the indigenous system of medicine for diuretic, cooling, acid, purgative, laxative, antibacterial, brain tonic and anthelmintic and burning sensation (Kusano et al., 2002).

Anti-HIV Activity of *Morus alba*

Traditionally the root bark of *Morus alba* is use in china for management of cough, asthma and other such diseases. Form *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 only HIV activity (Chen et al., 2005).

Antiallergic activity of *Morus alba*

According to Chai (2005) the anti-inflammatory activity showed by flavonoids and other related compound that were isolated from *Morus alba*. 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 activity (Butt et al., 2008).

Anticancer activity of *Morus alba*

The biochemical constituents viz. prenylated falvanone and 7,2,4,6-tetrahydroxy-6-geranyflavanone that were isolated from the root extracts of *Morus alba* exhibited antihepatomic activity, hepatoma is a primary malignancy of the liver. The anticancer activity also showed by biochemical constituent prenylated flavanone against rat hepatoma cells with an IC₅₀ of 52.8 mg/ml (Ercisli and Orhan, 2007). It also reported that the activity of COX-2 and inducible nitric oxide synthase (iNOS) inhibit by oxyresveratrol isolated from *Morus alba* at concentration of 10 mg/ml (Srivastava et al., 2006). From the root bark of *Morus alba* polysaccharide were isolated which decreases the production of antibody from the B cells and potentially increased lymphocyte proliferation. Such activities performed by *Morus alba* have important role in its anti-inflammatory potential (Manjula and Shubha, 2011). After performed experiment on the root bark of *Morus alba* Zhang (2009) isolated various type of biochemical constituents viz. glycosides, 5, 2, dihydroxiflavanone-7, 4-di-O-D-glucoside which inhibit cell proliferation of human ovarian cancer cell HO-8910 (Nadkarni, 1976). From the root bark of *Morus alba* various type of alkaloids and 1-deoxynojirimycin were also isolated that inhibit glycogenolysis, glycoprotein, processing and sacharide hydrolysis enzymes and the compound derived from it have a excellent therapeutic potential for the treatment of various kind of diseases viz. cancer, diabetes, obesity and viral infections (Mhaskar et al., 2000).

Antidiabetic activity of *Morus alba*

Morus alba has great importance by mean different aspects such as reduction in the absorption of blood glucose and reduction in the intake of food (Arya, 1997). There are some functional biochemical components viz. 1-deoxynojirimycin, polyhydroxylated piperidine alkaloids present in the bark and leaves of *Morus alba* which has a great potential to inhibit α -glycosidase (Shi-De, Nemeč and Ning, 1995). One of the experiment performed on human exhibit that the single oral administration of 1.2 g of DNJ- enriched powder significantly suppressed the elevation of postprandial blood glucose and the secretion of insulin (Chai et al., 2005). The root bark of *Morus alba* also exhibit hypoglycemic activity. When dose of 600 mg/kg/day of 70% alcoholic extract of the root bark of *Morus alba* given to the diabetic rat for 10 consecutive days the production of insulin increased by 44% and the amount of glucose reduced by 59% (Kofujita et al., 2004). Moran 20K is also present in aqueous methanolic extract of the root bark of *Morus alba* which is a protein it have the ability to lower the

blood glucose level in streptozotocin induced hyperglycemic mice model. Due to their composition moran 20K is also have a great importance because it contain above 20% serine and cysteine which is similar to insulin that further insures its chances of utilization in hyperglycemic patients (Chung et al., 2003). By using natural dietary supplements which containing 1-deoxynojirimycin and other α -glucosidase inhibitors in high concentration is of great potential interest to prevent the onset of diabetes and obesity (Choi and Hwang, 2005). After performed experiment on the *Morus alba* leaf extract Katsube (2006) recorded that due to the presence of deoxynojirimycene and its derivatives the *Morus alba* leaf extract act as a natural inhibitor of α -glucosidase (Prabhakar, 2012). Naukamura (2009) performed experiment on the *Morus alba* and find out that *Morus alba* also contain some other biochemical constituents like miglitol, boglibose, acarbose are the other inhibitor which are used in therapeutics. Lemus *et al.*, (1999) performed short term experiments on *Morus alba* and find that these plants exhibited hypoglycemic activity (Zhang et al., 2009). The glycosidase inhibitory activity exhibited by many alkaloids which are present in *Morus alba* (Kumar and Chauhan, 2008). The root bark of *Morus alba* contain some other chemical constituents like alkaloid, 1-deoxynojirimycin which inhibited glycoprotein, glycogenolysis, processing and sacharide hydrolysis enzymes where its derivatives have a great potential against cancer, obesity, diabetes and viral infection (Colonna et al., 2008). There are several nutritional components which are present in the leaves of *Morus alba* and they are the best feed for silkworm and also have been used in traditional Chinese medicine as an antihyperglycemic to treat and prevent diabetes mellitus. These nutritional components are steroids, flavones, amino acid, triterpenes, vitamins and some other trace minerals. In these nutrients those which containing sugar isolated, fagomine and 2- *O*- α -D-galactopyranosyl- DNJ (GAL-DNJ) have a great potential against hyperglycemic effects. The most extensively studied species *Morus alba* exhibited antihyperglycemic activity (Martin-Moreno, Soerjomataram and Magnusson, 2008).

Anti-inflammatory activity of *Morus alba*

According to Chai (2005) flavonoids and other related compounds which were isolated from *Morus alba* exhibited anti-inflammatory effects (Lee et al., 2002). *Morus alba* which is one of the most extensively studied species exhibited anti-inflammatory activity (Oku et al., 2006). The migration of leucocytes from the blood vessels to the flame sites is the fundamental feature of inflammation. The chemokine and its receptors can orchestrate leukocytes migration and also termed as chemotaxis (Kimura et al., 2007). Chemokines receptors caused many diseases and also have role in infection and inflammation. Consequently, the antagonists and inhibitors of chemokines and their receptors have become potential drugs targets for inflammatory diseases (Singab et al., 2005). Therefore the key target of the anti-inflammatory drugs has been proposed as a chemotaxis (Kim et al., 1999).

Antimicrobial Activity of *Morus alba*

The data regarding antibacterial activities of the black mulberry were poorly reported. So this research was stimulated due to the lack of references on its antibacterial activity (Asano et al., 2001). The biochemical constituents like mulberrofuran G, albanol B and Kuwanon C which are present in the root bark of *Morus* exhibited strong antibacterial activity with concentration 5-30 mg/ml of MICs. The strong effect reported by the constituent's sanggenon B, D and Morusin against only gramm positive bacteria (Katsube et al., 2006). It is also very effective to reduce lipid level, blood cholesterol and also have a great effect against arterial plaques, expectorant and diuretic (Nakamura, Nakamura and Oku, 2009). Lokegaonkar and Nabar (2010) find out that biofilm formation by *Streptococcus mutan*, *Streptococcus sanguinis* inhibited by the leaf extract *Morus alba* (Lemus et al., 1999). Manjula *et al.*, (2011) reported the antibacterial activity of HSP of DD, V1 and *Morus indica* species of mulberry (Dat et al., 2010). Against different type bacteria such as *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* the heat Stable Protein of *Morus alba* were tested and then compare with the antibiotic chlorempenicol, with the increase in the concentration of Heat Stable Protein the area of zone of inhibition were also increased for all the microbes tested by mulberry varieties. For *E.coli* MIC was at 25 μ l by *Morus alba* was more effective against

Escherichia coli at 100 µl (Kumar and Chauhan, 2008). In some other study the antimicrobial activity against different fungal strains and bacterial strains for petroleum ether, chloroform and methanol sequential leaf extracts of *Morus alba* at a various concentration of the extracts were tested. The zone of inhibition was determined against the microorganisms. Now the effects of these extract compared with the standard antibiotics, the results of the antibacterial activity and antifungal activity showed that all the extracts exhibited noticeable antibacterial activity and anti fungal in dose dependent manner against the microorganisms studied (Andallu et al., 2001). Omidiran *et al.*, reported that when ethanolic extract of *Morus alba* compared to the standard antibiotics it exhibited antimicrobial activity against a wider range of microorganisms (Singab et al., 2005). Different type of fraction of mulberry like acetic acid extract had strong antibacterial activities against *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* and fractions extracted chloroform had strong antimicrobial activity against *Bacillus subtilis* (Lemus et al., 1999). The bioactive molecules such as kuwanon C, Morusin and sanggenon B and D which extracted from the bark of *Morus alba* posses strong antimicrobial activity against various microorganisms such as *Streptococcus faecalis*, *Staphylococcus aureus*, *Mycobacterium semgmatis* and *Bacillus subtilis* and some molds species (Omidiran et al., 2012).

Antioxidant activity of *Morus alba*

The leaves of mulberry contain various chemical constituents viz. prenylflavanes and prenylflavane glycoside, quercetin 3-O-β-D-glucopyranosyl-(1/6)-β-D-glucopyranoside and quercetin reduce *in vitro* and *in vivo* oxidation process (Katsube et al., 2006). Through ferric reducing/antioxidant power assay the water extract of *Morus alba* leaves had the highest antioxidant properties (Kang, 2004). 5, 7-dihydroxycoumarin, 7-methyl ether and oxyresveratrol are present in the ethanolic extract of *Morus alba* and they are the scavenge superoxide and have antioxidant potential (Kimura et al., 1986). *Morus alba* contain biochemical constituents such as prenyl flavonoids coumarin and stilbene which exhibited hepatoprotective and free radical scavenging activities. The inhibitory effect showed by oxyresveratrol and mulberroside against FeSO₄/H₂O₂-induced lipid peroxidation in rat microsomes and scavenging effect on DPPH (1,1-diphenyl-2-picrylhydrazyl) radical (Barreiro et al., 2010). Arabshahi - Delouee and Urooj and Memon *et al.*, reported antioxidant properties of different extract of mulberry leaves (Proudfoot, 2002). A.A. Memon, N. Memon, D.L. Luthria, M. I. Bhangar, and A. A. Pitafi reported phenolic acid profiling and antioxidant potential of different mulberry leaves and fruits grown in Pakistan (Moser and Willimann, 2004). Katsube *et al.*, (2006) performed experiment on low-density lipoprotein antioxidant activity and extracted some compounds from *Morus alba* leaves (Kim et al., 1993). The biochemical constituents such as quercetin 3-(6-malonylglucosidase) and rutin are the chief flavonol glycosidase in the leaves of mulberry and these molecules are likely responsible for the bioactivities of the *Morus* plants. The antioxidant activity exhibited by oxyresveratrol, resveratrol and stilbenes constituents which were reported in the *Morus alba* (Krisch et al., 2008). Polyphenolic compounds are richly present in the *Morus alba* especially the flavonoids and the most significant for the antioxidant potential of mulberry plant is quercetin 3-(6-malanoglucoside) which is among flavonoids (Sohn et al., 2004).

Chen *et al.*, (2006) isolated and identified the anthocyanin component from *Morus alba* fruit to check their antioxidant activity and find out that cyaniding 3-glucoside and cyanidin 3-rutinoside are of valuable importance as antioxidants (Andallu and Varadacharyulu, 2003). According to Rossetto *et al.*, anthocyanin is a natural colorant constituent for the plant and it is present in the mulberry extract. By scavenging the peroxy radicals in tapering reaction the anthocyanin exhibited antioxidant activity (Doi, Kojima and Fujimoto, 2000).

Economic Importance of *Morus alba*

The leaves of *Morus alba* is not only well-known as food for silkworm, silk producing larvae of silkworm moth is *Bombyx mori*. But its other parts are also useful in making paper, furniture, textile, sculptures, medicines and musical instruments (Jang et al., 2002).

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