Review

Mulberry: Life enhancer

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Since old days, various plants are rich source of medicines. Ayurveda and other literature have claimed the different medicinal properties against certain serious diseases. Various researches have been conducted in last decades on different medicinal plants. The present review highlighted the potentiality of different medicinal properties of Morus species viz – Morus alba, Morus rubra, Morus serrata, Morus laevigata, Morus nigra, Morus macroura, Morus cathayana, Morus australis, Morus bombycis etc.

Key words: Mulberry, medicinal properties and biomolecules.

INTRODUCTION

Plants are exemplary source of medicines and several drugs have been derived directly or indirectly from them. Mulberry is the most medicinally important plant which belongs to genera Morus. It is a monoecious or dioecious plant up to 10 - 12 m high. This plant is widely distributed in India, China, Japan, North Africa, Arabia, South Europe etc. It helps in treatment of many serious diseases like diabetes mellitus, arthrosclerosis, hyperlipidemia; hypertension etc. The present review is based on active biomolecules having different medicinal properties of various Morus species. There are about a dozen of species found in genus Morus. Mulberry can be grown both in tropics and in the temperate regions. It is also raised in rainfed and irrigated conditions. The optimum temperature ranges from 24 to 29°C, atmospheric humidity from 65 to 80%.

Two species are native to the United States and rests are widely distributed throughout the warmer temperate regions of Eurasia, Africa, and North- America. These plants have a milky sap and bear the fruit for which they are named.

The White mulberry *Morus alba*, is renowned as the primary food source for silk worms and is widely cultivated in its native China. The fruit of white mulberry (which is also found in the Eastern United States) is white to pinkish, unlike the red or black berries of most other Morus species. According to sources, white mulberry is the species that has been used exclusively in Chinese medicine since A.D- 659. The Chinese Pharmacopoeia

(1985) lists the leaves, root bark, branches, and fruits as ingredients in medicinal preparations, but other parts, including the sap and wood ash, one also widely used.

The Morus plant is also a rich source of natural isoprenoid substituted phenolic compounds including flavanoids. These compounds have been studied by many investigators with structural, biological and pharmacological interests. Mulberry species are sources of series of isoprenoid - substituted phenolic compounds such as Kwanon G and H which have attracted from researcher's biosynthetic point of view (Nomura and Hano, 1994).

The methanolic extract of Morus species has anti-inflammatory, exudative, proliferative and anti-pyretic activities (Sener and Binjol, 1988; Jawad et al., 1988). Root bark having a bitter acid taste possessed cathartic and anthelmentic properties. Root is one of the constituents of drug named, "Glucosidase" which is used in high blood pressure. Root juice agglutinates the blood and is very useful in killing the worms in digestive system (Shivkumar et al., 1995).

The stem bark is used as purgative and vermifuge (Singh and Ghosh, 1992). The leaves are diaphoretic and emollient. Leaves juice keeps skin smooth, healthy and prevent throat infections, irritations and inflammations. The fruit juice of Morus species has refrigerant and laxative properties. It is also used as febrifuge, in diarrhoea, cold, endemic, malaria and amaeoebiosis (Shivkumar et al., 1995).

Commercial applications of mulberry in medicine

The main use of mulberry globally is as feed for the silk worm, but depending on the location, it is also apprecia-

ted for its fruit (consumed fresh, in juice or as preserves), as a delicious vegetable (young leaves and stems), for its medicinal properties in infusions (mulberry leaf tea), for landscaping and as animal feed. There are several places where mulberry is utilized traditionally as a feed in mixed forage diets for ruminants.

The sole use of mulberries in modern medicine is for the preparation of syrup, employed to flavors or colour any other medicine. Mulberry juice is obtained from the ripe fruits of the mulberry by expression and is an official drug of the British Pharmacopoeia. It is a dark violet or purple liquid, with a faint order and the refreshing, acid, saccharine test. The British Pharmacopoeia directs that Syrupus mori, chiefly used as an adjuvant rather than for its slightly laxative and expectorant quality, though used as a gargle, it will relive sore throat. The mulberry fruit is used for many medical purposes such as, to nourish the skin and blood, benefit the liver and kidney. It is also used to treat urinary incontinence, tinnitus, dizziness, constipation in the elderly and the anemic, to treat sore throat, depression and fever. The raw mulberry juice is squeezed out of the mulberry fruit with delicate fragrance and taste. This juice will enhance the health, such as yin nourishing, enriching the blood, notifying the liver and kidney, calming the nerves, promoting the metabolism of alcohol, balancing internal secretions, and enhancing immunity. Besides, the mulberry fruit can be brewed into wine and used as a resin substitute. This wine has a sweet and sour taste and cleans the blood. Many people believe that a glass of mulberry wine daily helps in getting rid of impurities and coprostasis (faecal residue in the intestines) in the body and enhance the health (Kumar. 2008). The fruits of M. alba are eaten fresh or made into juice, stews and tarts. They may be squashed and fermented to yield spirituals liquor. Besides, fruits are also potent source of anthocyanins which play key role in anti- oxidant activity. The finding also offers possible industrial use of mulberry as a source of anthocyanins as natural food colorant (Xueming et al., 2004), which could enhance the overall profitability of sericulture and also holds promise for tropical sericulture countries for profiting from industrial anthocyanins production from mulberry through better anthocyanins recovery.

Various combinations along with mulberry have been prepared for curing the diseases such as Cortex Lycii Radicis (du gu pi), Radix Glycyrrhizae Uralensis (gan cao) for cough with thick sputum, fever and irritability, Pericarpium Arecae Catechu (da fu pi) and Cortex Poriae Cocos (fu ling pi) for superficial edema with difficult urination etc. In Chinese markets, mulberry s often sold in the form of a paste called as Sangshengao. The paste is mixed into hot water to make tea to enrich the efficiency of the liver and kidney and sharpen the hearing and brighten eyes (Masilamani et al., 2008). This offers a challenging task to the mulberry germplasms resources across the globe, in exploration and collection of fruits yielding mulberry species; their characterization, cata-

loguing and evaluation of such ingredients by using traditional as well as modern means and bio technology tools; developing an information system about these mulberry species; training and global coordination of utilization of these genetic stocks and finally in evolving suitable breeding strategies to improve the several active biomolecules in the potential breeds by collaboration with various research stations in the field of sericulture, plant genetics, breeding, biotechnology and pharmacology (Table 1).

Morus alba L. white mulberry

A medium sized, monoecious, deciduous tree with bark of large stems, brown, rough, height of about 30 and 1.8 m in girth indigenous to China and in hilly areas of Himalayas up to an elevation of 3300 m. The root is astringent and bark is anthelmintic (Bhattari, 1992). Root is one of the constituent of Chinese drug named "Sohaku-hi" which reduces the plasma sugar level in mice (Hikino et al., 1985). Decorked bark is used against chronic bronchitis and emphysema.

The ethyl acetate extract of root bark contains four hypotensive Diels Alder adducts named as Kwanon I, Kwanon I hexamethyl ether, Kwanon I octamethyl ether, 2'-Hydroxy-2,4,4'-trimethoxychalcone and 2'-Hydroxy 3' prenyl-2,4,4'-trimethoxychalcone III were isolated and reported by (Taro and Toshio, 1982) .

Chinese people named it as "Sang bai Pi, the root bark of *M. alba* is a traditional Chinese medicine which is used as medical treatment for cough, asthma and other diseases. The ethanolic extract of Sang Bai Pi displayed activity HIV which contains flavnoids like Morusin, Mulberrofuran D, G, K and Kwanon G, H., of which Morusin and Kwanon H showed positive activity against HIV (Shi-De et al., 1995). Morusin also inhibits tumor promotion (Shigeru et al., 1989).

Root is one of the constituent of a Chinese drug named "Sohaku hi" which reduces the plasma sugar level in mice (Hikino et al., 1985). A novel stilbene glucoside was isolated from root bark of *M. alba* along with Mulberroside A, Cis-mulberroside A and Oxyresveratrol (Feng et al., 1996). Kwanon G was isolated from ethyl acetate fraction of methanolic extract of *Morus alba* which showed antibacterial activity against *Streptococcus mutans, Streptococcus sobrins* and *Streptococcus sanguis* (Park et al., 2003).

Four new antifungal phytoalexins- Moracin E, F, G and H, Kwanon D, E, F were isolated from root bark of mulberry plant. The root bark of *M. alba* contains Sanggenon alkaloid which inhibited plaque formation. Morusin 4'-glycoside and Kwanon H show positive activity against HIV. The root bark also contain an alkaloid, Deoxynojirimycin-1 inhibited glycogenlyses, glycoprotein, processing and saccharide hydrolysis enzymes whereas its derivatives have great therapeutic potential for the treatment of viral infections, diabetes, obesity and cancer

Table 1. Active biomolecules of different Morus species

SI. No.	Name of Morus species	Active constituents	Plant part used	Medicinal Properties
1.	Morus alba	Kwanon I, Kwanon I hexamethyl ether, Kwanon I octamethyl ether,2'-Hydroxy - 2,4,4'-trimethoxychalcone and 2'-Hydroxy 3' prenyl-2,4,4'-trimethoxychalconeIII, Mulberrofuran T and Kwanon E, Morusin, Mulberrofuran D, G, K, Kwanon G, H, Mulberroside A, Cis-mulberrosideA, Oxyresveratrol, Isoquercetin, Kwanon G, Moracin E, F, G and H, Kwanon D, E, F, Deoxynojirimycin-1 etc.	Root, stem, leaves, fruit	Astringent, anthelmintic, HIV, cough, anti – inflammatory, exudative, high blood pressure, diaphoretic, purgative, emollient, diahorrea, diabetes, atherosclerosis, anti-tumor, hypoglycemia etc.
2.	Morus australis	Australone A, triterpenoid 3β-[(m-methoxy benzoyl) oxy] urs-12- en-28- oic acid, morusin, Kwanon C, betunilic acid, β-amyrin, querecetin ursolic acid, Mulberrofuran D, sanggenols N and O etc.	Root, Leaves, fruits	Astringent, anthelmintic, purgative, anti-platlet etc.
3.	Morus bomycis	N-methyl-1-Deoxynojirimycin, Kwanon G,H, Moracin A-Z, Albanins A-H, γ- aminobutyric acid, L-asparagine, L-arginine, L- lysine, choline, Mulberrofuran I	Root, Leaves	Hypotensive,anti-microbial, diabetes, HIV, antipholigistic, diuretic etc.
4.	Morus laevigata	Citrulline, hydroxyprolines, free amino acids	Fruit	plaster for sores , cools the blood ,
5.	Morus nigra	Deoxynojirimycin	Root, leaves, fruits	diabetes, AIDS, purgative, arterial pressure, vermifuge, cancer etc.
6.	Morus serrata	β -Amyrin acetate, betunilic acid, cerylalcohol, querectin and morin	Root	-
7.	Morus rubra	Rubraflavones A,B,C,D	Root	Anti-dysentric, laxative, purgative vermifuge, urinary problems weakness etc.
8.	Morus macroura	Guangsangons A -N, albafuran C, Kwanon J,X,Y, Mulberrofuran G, K. J	Stem	anti –inflammatory , anti- oxidative
9.	Morus cathayana	Sanggenols F, G, H, I, J, K cathayanon. A,B,	Root	anti –inflammatory , hypertension etc.

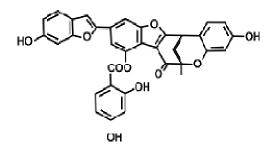


Figure 1. Mullberrofuran M

(Hughes and Rudge, 1994) (Figure 1 - 3)

Morus alba cortex is also one of the constituent of herbal mixture named 'Jiang Qi Ding Chuan San' which has longer and better bronchodilatory effect in asthmatics. The leaf contains 22 - 23% protein and yield leaf human nutrition (Singh, 1997). They also contain flavone protein concentration (5 - 6 g/100g fresh it). The protein

Figure 2. Kwanon Y

has future supplementary protein food sources for glycosides, astragalin, isoquerecetin, querecetin 3-o (6'-o-acetyl)- β -D-glucoside. The acetylated glycosides have moderate inhibitory effect on water-insoluble glucon synthesis by glucosytransferase. The ethanolic extracts of mulberry leaves exhibited moderate antimicrobial activity

Figure 3. Kwanon Z.

Figure 4. Moracin C.

Figure 5. Moracin D.

activity against Staphylococcus aureus, Bacillus subtilis and Pseudomonas aeruginosa. Hot water extract of dried mulberry leaves fed to rabbits on 1% cholesterol diet exhibit significant hypolipidaemic or hypocholestroemic effect. In addition, hepatic enlargement and fat deposition in hepatic cells was also observed. The mulberry leaves exhibited a potent hypoglycemic activity in fasted and non-fasted STZ diabetic mice and glucose level fell by 24.6 \pm 6% and 81.4 \pm 7.9% respectively (Grover et al., 2002). The 1-butanol extract of mulberry leaves inhibits the oxidative modification of low density lipoprotein and prevent against atherosclerosis (Kayo et al., 2000) .The active biomolecules which play vital role in oxidative modification is Isoquercetin. Another two new Diels Alder adduct were isolated form callus tissues of leaves of M. alba named as Mulberrofuran T and Kwanon E (Hano Yoshio et al., 1989).

The fruits are eaten fresh or made into juice, stews and tarts; they may be squashed and fermented to yield spirituous liquid. Analysis of fruit contain moisture 8.75%, protein 1.5%, fat 0.4%, carbohydrate 8.3%, fiber 1.4%, mineral matters 0.9%, calcium 80mg, phosphorus 40 mg, iron 1.9 mg/100g, carotene (as vitamin A) 1.74%, thia-

thiamine 9 μg , nicotinic acid 0.8 mg, riboflavin 184 μg and ascorbic acid 13mg/100g. The fruits also contain a flavanoids, possibly eriodictyol.

The fruit of *M. alba* has a cooling and laxative property and are used throat, dyspepsia and melancholia. Ripe fruits are appetizer and carminative. Fruits are also used in loss of appetite, flatulence, constipation and intestinal worms like tapeworm. Syrup of ripe fruits is useful in heart diseases, bleeding disorder, burning sensation, debility and antiaging. Decoctions also prepared from the fruits are used against cerebral arteriosclerosis, chronic nephritis, kidney asthenia, alopecia areata, central retinitis and nasopharyngeal cancer. The pollen extract cause an air-borne contact urticaria. The plant is also a part of composite drug which is used for the treatment of tonsillitis (Singh, 1997).

Morus australis Poir syn. Morus acidosa griff

It is a shrub or small tree found in Assam and Khasi hills. The roots are astringent and anthelmintic where as the bark is purgative. Leaf decoction is given as a gargle to soothe inflamed vocal cords (Jain and Fillips De, 1991). The fruits are used to alleviate fever. The plant extracts was very effective in inhibiting the both of growth of serotypes C and D of *Streptococcus mutans* and gram + ve bacteria (Chen et al., 1989).

A new prenyl flavnoid australone A(1), triterpenoid 3β -[(m-methoxy benzoyl) oxy] urs-12- en-28- oic acid (2), morusin (3), Kwanon C(4), betunilic acid, β - amyrin, querecetin ursolic acid, of which Morusin (3) showed significant role on arachidonic acid, collagen and prenyl-flavnoid induced platelet aggregation. Mulberrofuran D and phenolic constituent like Sanggenols N and O were isolated from root bark (Shi et al., 2001) (Figures 4 and 5).

Morus bombycis koidz

This plant is found in China, Japan, Korea and Southern Sakhaline. Root bark contains quinones named as Kwanons G and H with hypotensive activity, phytoalexins like Moracin A-Z and Albanins A -H with anti-microbial activity. The leaves also contain N-methyl- 1 –deoxynojinimycin which is used against diabetes mellitus. This compound is also inhibits the infectivity of human immuno deficiency virus (Asano et al., 1994) (Figure 6 – 8).

From water extract of root bark of *Morus bombycis* koidz, seven compound namely γ - aminobutyric acid, L-asparagine, L-arginine, L- lysine, choline etc were isolated which are active against microbial and hypotensive activity (Daigo et al., 1986). From acetone extract of root bark of *M. bombycis* a 2-arylbenzofuran derivative was isolated and named as Mulberrofuran I (Yoshio et al., 1982). Root bark is an antipholigistic, diuretic and expectorant. Mulberrofuran C, a new 2-aryl benzofuran derivative along with six known flavonoids derivative like

Mulberrofuran D

Figure 6. Mulberrofuran D.

Figure 7. Albanol A

Figure 8. Albanol B

Morusin, Cyclomorusin, Kwanon C, E, G, and H were isolated from root bark extract of *M. bombycis* (Taro and Tsutomu et al., 1982).

Morus laevigata wall .ex Brandis

A tree found in outer Himalayas from Kumaon eastwards to Assam. Bark is dark brownish grey in color when young, leaves are ovate-cordate, flowers small, fruits long cylindrical, yellowish white, sweet or insipid. The milky juice of fruit is used as a plaster for sores and cools the

blood. Rapid clonal propagation is possible through *in vitro* culture of nodal explants. Brandis was the best cytokinin for shoot multiplication.

The fruits are rich in citrulline and hydroxyprolines. The seeds are rich source of free amino acids (Ali and Qadri, 1987).

Morus nigra Linn. Black Mulberry

A medium or small sized tree 6 - 9 m high, native of West Asia. It is also cultivated in Kashmir, Darjeeling, leaves are ovate-cordate, flower dioecious or monoecious, fruits are syncarp, ovoid, 2.0 - 2.5 an long, purple to black, juicy, edible. The root bark is purgative and vermifuge. Root has and effect on pancreas and glycogenylsis while its juice reduces the blood sugar level in diabetic patient. The root bark extract contains Deoxyjirimycin (DNJ), an alkaloid which said to have active against AIDS virus. An infusion of leaves causes a drop in blood sugar (Singh and Ghosh, 1992), sometimes diuresis and a reduction of arterial pressure. The fruits are one of the constituent of Unani medicine named "Tut- i-aswad" which is said to be against cancer (Ahmad et al., 1985).

The bark is purgative and vermifuge. Root bark contains calcium malate; the bark contains tannins, phytobaphenes, sugar, phytosterol, (m.p.132°), ceryl alcohol, fatty acids and phosphoric acid. Analysis of ripe fruits gave the following values: moisture 85.5%, protein 0.7%, fat 0.4%, carbohydrates 12.2%, fibre 0.8%, and mineral matter 0.4%, calcium 60 mg., phosphorus 20 mg, iron 2.6 mg/100g., thiamine 58 μg , nicotinic acid 0.2 mg, riboflavin 92 μg , ascorbic acid 10 mg/100g.

Morus serrata Roxb

It is a large tree 18-21 m high, with a clean cylindrical bole 3.5 m long, found from Trans Indus to Kumaon, principally in the inner regions of Himalayas at an altitude of 1200-2700 m. Bark is reddish or grayish brown, leaves ovate-cordate, flowers dioecious, fruits long, sweet and edible. The bark of *Morus serrata* contains β Amyrin acetate, betunilic acid, cerylalcohol, querectin and morin (Chemical Abstracts, 1979)

Morus rubra Linn Red Mulberry

This plant grows up to 18m high, found in North America. The roots are catharic or emetic and are used as antibilious and by human when passing yellow urine. The bark has antidysentric, laxative, purgative and vermifuge properties and is used for urinary problems and weakness (Duke, 1992).

Four new flavones namely rubraflavones A, B, C and D - isolated and their structures are given below (Rastogi and Mehrotra, 1990) (Figures 9 and 10).

Figure 9. Rubraflavone A, Rubraflavone A and Rubraflavone Δ

Figure 10. Rubraflavone D

Figure 11. Cathayanon A

Morus macroura

This mulberry plant belongs to economically and medically important genus Morus. Previously, many novel compounds, which were regarded biogenetically as Diel Alder adducts of dehydroprenylphenol and chalcone

Figure 12. Cathayanon B

which were isolated from M. *alba*, *M. bombycis*, *Morus Ihou*. About 9 compounds have been isolated from its ethanolic extract against oxidative and inflammatory effects which are named as Guangsangons A, B, C, D and E along with four known compounds - Albafuran C, Kwanon X, P, Y from *Morus macroura*, of which compound Guangsangons A, Albafuran C, Kwanon X showed good anti-oxidative activity while Guangsangons A, B, D, showed activity against inflammation (Yu- De-Quan et al, 2004).

Five Diels Alder Type Adducts named Guangsangons F, G, H, I and J along with two known compounds Mulberrofuran J and Kwanon J were isolated from ethanolic extract of stem bark of *Morus macroura* which exhibit potent anti –oxidant and anti-inflammatory activities (Yu De-Quan et al., 2004).

The ethanolic extract of stem bark of *M. macroura* results in isolation of Diels Alder Type Adducts Guangsangons K-N together with Mulberrofuran G and K. The new isolated structures showed good anti-oxidant activity (Yu De-Quan et al., 2004).

Morus cathayana

It is Chinese mulberry trees which have several compounds that are actively participating for curing the disease hypertension. On further examination of root bark of *Morus cathayana*, five new flavnoids Sanggenols F, G, H, I, J etc. was isolated. The other two new Diel- Alder type adduct, Cathayanon. A and B which resembles to compound sanggenon C & O which were also isolated from root bark of *M. cathayana* that plays a vital role in anti-inflammation(Rui-Chao and Lin Mao, 2001).

Another four new prenylated flavones namely Sanggenols F-K was isolated from root bark of *M. cathyana* (Toshio et al., 1998) (Figures 11 and 12).

Recent researches against certain serious diseases

The health giving properties of mulberry leaf are recognized for its diuretic, blood sugar and blood pressure reducing effects. New pharmacological benefits of mul-

berry leaf against serious diseases like Alzheimer's disease, atherosclerosis, hyperlipidemia.

Against Alzheimer's disease

Alzheimer's disease produces general mental enfeeblement loss of memory, reason and often feeling and dementia in a person. Evidence suggests that amyloid beta-peptide (1-42) plays an important role in the etiology the disease, forming plaques and fibrils disturbing the neuron network in the brain. The result suggests that mulberry extract provide viable treatment Alzheimer's disease through inhibition of amyloid beta- peptide (1-42) fibril formation and attenuation of neurotoxicity induced by amyloid beta- peptide (lyengar, 2007).

Prevention of Atherosclerosis

Atherosclerosis is the deposition of hard yellow plaques of lipid material (cholesterol) in the inner layers of arteries, causing coronary thrombosis or heart- attack. Very Low Density Lipoprotein (VLDL) so called good cholesterol and removes excess cholesterols from blood and carries to liver.

Harauma and his co-workers from Kyoto, Japan fed mulberry leaf powder to apolipoprotein E-deficient mice. The mice were fed either normal or chow or a diet containing one percent mulberry leaf powder from six weeks of age. A significant increase in lag time of lipoprotein oxidation was detected in mulberry leaf group. The results confirm that mulberry leaf contains anti-oxidative substance that might help prevent atherosclerosis (lyengar, 2007).

Controlling hyperlipidemia

Total flavnoids were isolated from mulberry leaves (MTF) and were evaluated on mice with high cholesterol (Hyperlipidemia) induced by a chemical triton WR-1339. After 12 h, serum lipid levels were reduced significantly. The triglycerides (TG), Total cholesterol (TC), low density cholesterol (LDL-C) were remarkably reduced to 388, 257 and 189 mg in mulberry leaves treated mice compared 540, 464, 299 mg/100ml respectively in group treated triton WR-1339. The ratios of HDL -C /TC, HDL-C/ LDL -C were increased to 0.42 and 0.57 against 0.33 and 0.52 respectively (Iyengar, 2007).

Glucosidase inhibitor Deoxynojirimycin in mulberry

Mulberry 1-dexoynojirimycin (DNJ) is a potent source alpha-glucosidase inhibitor and helpful to establish greater glycemic control in type 2 diabetes. Young mulberry leaves taken from top part of branches in summer contains the highest amount of DNJ. In a human study, DNJ enriched powder of mulberry leaves significantly

suppressed elevation of post-prandial glucose. Newly developed DNJ enriched powder can be used as a dietary supplement for preventing diabetes mellitus (lyengar, 2007).

It is evident that large number of active biomolecules that are present in different species of mulberry like *M. alba, M. rubra, M. serrata, M. laevigata, M. nigra, M. macroura, M. cathayana, Morus australis, M. bombyx etc.* provides an all together new world for life enhancement as they posses high degree of health and therapeutic values. Thus mulberry could be explored and exploited further for enhancing the life potential among all

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