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Chemical composition and pharmacological functions and principles of mulberry: A Review

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Abstract
Mulberry, Morus spp. of the family Moraceae being the primary food plant for the monophagous insect *Bombyx mori* has special significance in sericulture industry. The present review is based on active biomolecules having different medicinal properties of various Morus species. Due to its chemical composition and pharmacological functions it is also being utilized as a medicinal plant. Many active compounds have been isolated from the mulberry plants which are used as medicines. Biochemical compounds such as Moranolin (deoxynojirimycin (DNJ)), Moran (glycopeptides), hydrophobic flavonoids (flavones and flavonone), 2 arylbenzofuran, and ethanolic extract, flavonoids, polyphenols, carotenoids, vitamin A, vitamin C, vitamin E, ethyl acetate, γ -aminobutyric acid, flavanics are isolated from different parts of mulberry plants which have hypoglycemic, anti-obesity, lipid-lowering, antioxidants, antiinflammatory, antiallergic, vasoactive, neuroprotective and anticancer action activity. Mulberry plants are identified for their profitable health consequences and therefore drawn the attention of the pharmaceutical industry. The main objective of present review is to reveal the pharmological function and active principles present in Mulberry plants.

Keywords: Antioxidants, flavonoids, hypoglycemic activity, moranolin, mulberry, pharmaceutical industry

1. 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, grows up to 10 - 12 m height. 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. 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 per cent.

The genus *Morus* contains approximately 16 members of family Moraceae, occurring primarily in northern temperate regions with some extending into tropical areas of Africa and the South America. There are 11 species distributed widely in China. Genus *Morus* (Mulberry) is one such example that consists of over 150 species, among these, *M. alba* is dominant (Srivastava *et al.,* 2006) [32]. Generally, it is used as foliage to feed the silkworms (*Bombyx mori*) In many countries like Turkey and Greece, *M. alba* and other Mulberries are grown for fruit production.

2. History
Over the years, medicinal plants have been found useful in the treatment and management of various health problems. About 80% of the world population relies on the use of traditional medicine, which is predominantly based on plant material (WHO, 1993) [36]. Scientific studies available on a good number of medicinal plants indicate that promising Phytochemicals can be developed for many health problems (Gupta *et al.,* 1994) [10]. Plants produce a diverse range of bioactive molecules, making them a rich source of different types of medicines. A rich heritage of knowledge on preventive and curative medicines was available in ancient scholastic works included in the Atharva veda, Charaka, Sushruta etc.

Over 50 per cent of all modern clinical drugs are of natural product origin (Stuffness and Douros, 1982) [34] and natural products play an important role in drug development programs in the pharmaceutical industry (Baker *et al.,* 1995) [4]. Herbal drugs have gained importance in recent years because of their efficacy and low cost.

Medicinal plants play an important role in Indian ayurvedic system of medicine and many active compounds were isolated from the plants by researchers which are being used as medicines. These active compounds are in nature which is known as phytochemical or secondary plant products. Mulberry plant is one of conventional herbs which are used in medicine from centuries ago due to its chemical composition and pharmacological function. All most all parts of mulberry plants are used as medicine in Chinese and Indian medicine. According to Singh *et al.,* (2008) [30] active principles which are isolated from medicinal plants may influence health and inhibited the bacterial or fungal pathogens. According to Zou and Chen (2003) [39] mulberry leaves contain N-containing sugars, rutin, quercetin, volatile oil, amino acid, vitamins and microelements, which have so many pharmacological activities such as reducing blood glucose, antihyperlipidemia, hypertensive, bacteriostasis and antivirus. Andallu *et al.,* (2001) [1] and Andallu and Varadacharyulu (2002) [2] have reported many different medicinal properties of mulberry leaves. According to Maria (2008) [22] root extract of mulberry plants is also having antimicrobial activity. Bio active compounds in different species of mulberry can enhance life (Venkatesh and Chauhan, 2008) [35]. Different pharmaceutical properties of mulberry plants are reviewed by Singhal *et al.,* (2010) [31]. They found that 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. The medicinal properties of mulberry plants are identified for their profitable medicinal value and therefore attracted the attention of the pharmaceutical industry. The main objective of present review is to discuss the active principles of Mulberry plants relating to its pharmacological activity to human diseases.

3. Pharmacological activity to human diseases

3.1 Hypoglycemic activity

Hypoglycemia is a condition that occurs when blood sugar level is too low in body. Diabetes mellitus is caused by the ineffectiveness of the insulin produced by pancreas. Due to inadequacy of insulin secreted by pancreas the concentration level of glucose increase in blood which harm many body systems in specifically the blood vessels and nerves. So far medicinal plants have been recommended for treatment of diabetes. From the centuries ago most of the countries of world practiced the traditional medicinal systems which are based on herbal plants. Mulberry was used in old Chinese herbal medicine for reducing blood serum glucose (Andallu *et al.,* 2001) [1]. Both leaves and roots extracts of mulberry plants are having hypoglycemic properties and it is used in the treatment of diabetes (Andallu and Varadacharyulu 2002, Kelkar *et al.,* 1996) [2, 17]. Mulberry plants contains moranolin (DNJ), Moran (glycopeptides), hydrophobic flavonoids (flavones and flavonone) which play main role in hypoglycemic action (Singab 2005, Fallon 2008) [29, 8]. Katsube (2006) [15] conducted a study on mulberry leaf extract and found that mulberry leaf extract acts as a natural inhibitor of α-glucosidase due to deoxynojirimycin (DNJ) and its derivatives.

3.2 Anti-obesity action

Obesity is defined as an abnormal or extravagant fat accumulation that extant a risk to health. Obesity is related with the diabetes, hypercholesterolemia, hyperlipidemia, hepatic steatosis, and atherosclerosis. Decrease the amount of sugars absorbed has consequences for body weight. Oh (2010) [25] conducted a short term study on mice and exhibited an antagonistic action of mulberry extract on melanin concentrating hormone receptor, which help in decrease in body weight. They also suggested that ethanolic extract obtained from mulberry leaves showed anti-obesity action on diet-induced mice.

3.3 Hyperlipidemia action

Hyperlipidemia is characterized by excess cholesterol and fatty substances in the blood. Hyperlipidemia is a risk factor for heart disease. *Diabetes mellitus* is related with different kinds of lipid peculiarity. According to Andallu (2009) [3] Lipemia, cholesterol, especially LDL (low-density lipoprotein) and VLDL (Very-low-density lipoprotein) cholesterol are engaged in the growth of atherosclerosis and related abnormalities. Andallu *et al.,* (2009) [3] reported that the mulberry leaf ingredient governed glucose and improved the lipid abnormalities related with highly capable diabetes in STZ-diabetic rats with anti lipids and antioxidant action. Mulberry leaf extracts contains large quantity of flavonoids which work as the scavenger of blood lipid radicals. Li *et al.,* (2005) [20] conducted study on rats and found that mulberry leaf extract which is rich in flavonoids, work as the scavenger of blood lipid radicals in sugar metabolism and antioxidation in rats. According to Liu *et al.,* (2009) [21] Mulberry extract showed the hypolipidemic effects which elevate (Low-density lipoprotein receptor) LDLR gene expression and the clearance proficiency of LDL (Low-density lipoprotein) and a decline in the lipid biosynthesis. Andallu *et al* (2001) [1] conducted a study on mulberry plants and found that mulberry is capable of lipid peroxidation. They observed a consequential reduction in plasma, erythrocyte membrane, and urinary peroxidase of diabetic patients with mulberry therapy. According to Andallu and Varadacharyulu (2002) [2] mulberry leaves are delicious and capable in governing hyperglycemia and glycosuria in STZ-diabetic rats. They found that mulberry leaves have ability to quick protective outcome against lipid peroxidation by scavenging oxygen and enhance the function of antioxidant enzymes by integrity of antioxidant flavonoids (quercetins and moracins) present in the leaves and also suggested that the increased oxidative stress in diabetic rats was reduced by the mulberry leaves. According to Singab (2005) [29] extracts from the root bark of mulberry tree contains some components which showed hypoglycemic function, had defensive consequences on pancreatic β cells, obstruct their degeneration and decreased lipid peroxidation.

3.4 Antioxidants action

Antioxidants inhibit the oxidation process in the plant and animal organisms and play a vital role in phyto physiological process. Antioxidants are widely used in the food and drink that are regularly served or consumed and have been systematically examined for the prevention of diseases such as cancer, heart disease and general sickness.

Andallu (2009) [3] reported that the mulberry plants contains many active compounds which acts as an antioxidant like polyphenols, carotenoids and vitamin A, C & E. They found that these compounds increase the body's antioxidant status and regulate Low-density lipoprotein (LDL) oxidation through different mechanisms. Hong *et al.,* (2004) [11] found that mulberry fruits increase the strength of the antioxidative protecting system and diminish the damaging oxidative substances in the red blood cells (RBCs) of diabetes induced rats. Katesube *et al.,* (2006) [15] conducted a study on Low-density lipoprotein (LDL) antioxidant activity and extracted some compounds from mulberry *M. alba* L. leaves. They found that quercetin 3-6-malonylglucoside and rutin are the chief flavonol glycosides in the mulberry leaves. Kim *et al.,* (1999) [18] isolated nine flavonoids from mulberry leaves and examined for their free radical scavenging function and confirmed to be antioxidative.

3.5 Anti-inflammatory and antiallergic actions

Anti-inflammatory term generally used for the property of substances that reduces swelling. The use of anti-inflammatory herbs for health improvement has a long and successful history in traditional medicine. Plants synthesize complex, organic molecules for their structure and function, and are therefore a rich source of chemicals which often have health enhancing properties. According to Chatterjee (1983) [7] mulberry leaves were reported to having antipyretic and anti-inflammatory effects. According to Chai (2005) [6] flavonoids and related compounds isolated from *Morus alba* exhibited anti-inflammatory effects. They found that hot water extract from the bark of *Morus alba* root has strong antihistaminic and antiallergic activity.

3.6 Vasoactive and neuroprotective action

Vasoactive effects result in either increasing or decreasing blood pressure. According to Xia *et al.,* (2008) [37] ethyl acetate extract from leaves of *Morus alba* showed vasoactive effect on studies in isolated rat thoracic ring. Mulberry juice showed anti-stress activity against mice, which inhibited the elevation of plasma lipid peroxide levels induced by stress (Sakagami *et al.,* 2006) [27]. Morin, a flavonoids found in mulberry reduced the tissue level cyclosporine and act as immunosuppressive agent with narrow therapeutic range and minimize the nitric oxide production by the activated macrophages (Fang *et al.,* 2005) [9]. According to Kang *et al.,* (2006) [14] mulberry fruit contains the cyanidin-3-O-β-D-glucopyranoside which prevents the neuronal cell damage. They also suggest that mulberry fruit extracts having neuroprotective properties and prevent the cerebral damage caused by oxygen glucose deprivation (OGD) in PC12 cells. The anaerobic treatment of mulberry leaves makes γ-aminobutyric acid to enhances the neuro-protection effect against *in vivo* cerebral ischemia (Kang *et al*., 2005) [13]. The effectiveness of *Morus alba* in improving the vascular reactivity of diabetic rats, the mechanism of which may associate with the abatement of oxidative stress (Naowaboot *et al*., 2009) [24].

3.7 Anticancer action

Many medicinal plants have anti-bacterial, anti-viral, anti-inflammatory, anti-cancer, immunostimilatory and antioxidant properties as well as compounds which affect specific organs. Singh *et al.,* (2010) [31] stated that the methanolic extract of mulberry leaves shows efficient cytotoxic behavior against cancer cells. They identified many compounds like kuwanon S, 8-granilapigenin, ciclomulberrin, ciclomorusin, morusin, atalantoflavones, kaempherol with the action strong cytotoxic cell lines HeLa, MCF-7 and Hep3B. Zhang (2009) [38] conducted a short-term study on root bark of *Morus alba* and isolated a flavanics *i.e*. glycoside, 5,2 '-dihydroxiflavanone-7, 4'-di-O-D-glucoside, which prevents cell proliferation of human ovarian cancer cell HO-8910. Therefore we suggest that mulberry plant is a ―kalpavraksha‖ which can be utilized for making silk and pharmaceutical's. Further research is needed for highly useful medicinal properties.

4. Conclusions

Mulberry plant is one of the traditional herbs which is used in medicine from centuries before. Due to its pharmacological properties mulberry is used as medicine currently in many countries. Mulberry is proved in protecting liver, improving eyesight, facilitating discharge of urine, lowering of blood pressure, anti-diabetic and controlling weight in humans as well as animal models. It is the need of the hours to explore its medicinal value by Indians.

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39. ZOU Sheng-qin, CHEN Wu. A review on chemical constituents, pharmacological activity and application of mulberry leaves, journal of Chemical Industry of Forest Products (Bimonthly) 2003-01 Table 1: Active Compounds in mulberry plant, 2003.