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History and active pharmacokinetic 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 which has special significance in sericulture industry. Due to its chemical composition and pharmacological functions it is being utilized as a medicinal plant. Many active compounds isolated from the mulberry plants which used as medicines. Biochemical compounds such as Moranolin (DNJ), Moran (glycopeptides), hydrophobic flavonoids (flavones and flavonone), 2-Arylbenzofuran, and Ethanolic extract, Flavonoids, Polyphenols, Carotenoids, Vitamins A, C, E, Ethyl acetate, γ -aminobutyric acid, Flavanics are isolated from different parts of mulberry plants which play a vital role in Hypoglycemic activity, Anti-obesity action, Lipid-lowering action, Antioxidants action, Anti-inflammatory actions, Antiallergic action, Vasoactive action, Neuroprotective action, Anticancer action. Mulberry plants are identified for their profitable health consequences and therefore attracted the attention of the pharmaceutical industry. The main objective of presentreviewis to provide the active principlesof Mulberry plants.**

***Keywords*—Antioxidants action, Flavonoids, Hypoglycemic activity, Moranolin, Mulberry, Pharmaceutical industry.**

I. HISTORY

Medicinal plants play an important role in Indian ayurvedic system of medicine and many active compounds were isolated from the plants by researchers which used as medicines. These active compounds are chemically 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. Most of the parts of mulberry plants are used as medicine in Chinese and Indian medicine. According to Singh et al., (2008) active principles which are isolated from medicinal plants may influence health and inhibited the bacterial or fungal pathogens.Mulberry is a fast-growing deciduous plant that grows under various conditions i.e., tropical, subtropical and temperate (Srivastava et al., 2003). Mulberry belongs to the family of moraceae and genus morus usually cultivated to feed silkworm for manufacturing of silk.*Morusalba* (white mulberry) and *Morusindica* (Indian mulberry) are the most popular species of mulberry. According to Zou and Chen (2003) mulberry leaves contain N-containing sugars, rutin, quercetin, volatile oil, amino acid, vitamins and microelements, which have so many pharmacological activies such as reducing blood glucose, antihyperlipidemia, hypertensive, bacteriostasis and antivirus. Andallu et al., (2001) and Andallu and Varadacharyulu (2002) have reported many different medicinal properties of mulberry leaves. According to Maria (2008) 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). Different pharmaceutical properties of mulberry plants are reviewed by Singhal et al., (2010). 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 pharmacokinetic activity to human diseases.

II. 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). 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).Mulberry plants contains moranolin (DNJ), Moran (glycopeptides), hydrophobic flavonoids (flavones and flavonone) and 2-arylbenzofuran which play main role in hypoglycemic action (Singab 2005, Fallon 2008). Katsube (2006) 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. According to Nakamura (2009) acarbose (Glucobay), miglitol (Diastabol), boglibose are other inhibitors which are used in therapeutics. Lemus et al., (1999) conducted short term experiments and reported hypoglycemic activity of dried levels of a *Bauhinia ulrifolius*, *Galegaofficinalis*, *Morusalba* and *Rubusulnifolius.* Sachdewa and Khemani (2003) reported hypoglycemic activity of an ethanol extract of the flower of *Hibiscus rosasinensis* on diabetes-induced rats. Table.1 shows the important active compounds occurs in mulberry plants.

III. ANTI OBESITY ACTION

Obesity is defined as abnormal or extravagant fat accumulation that extant a risk to health. An obese person has accumulated so much body fat that it might have a negative effect on their health. Obesity is related with the diabetes, hypercholesterolemia, hyperlipidemia, hepatic steatosis, and atherosclerosis and decrease the amount of sugars absorbed has consequences for body weight. Oh (2010) 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.

IV. HYPERLIPIDEMIA ACTION

Hyperlipidemia is a 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)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) conducted a study on rats and found that 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) 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) 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) conducted a study on mulberry plants and found that mulberry is capable of against lipid peroxidation when compared with glibenclamide treatment. They observed a consequential reduction in plasma, erythrocyte membrane, and urinary peroxides of diabetic patients with mulberry therapy. According to Andallu and Varadacharyulu (2002) 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 O_2 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) 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.

V. 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. According to Andallu (2009) 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) 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) conducted a study on Low-density lipoprotein (LDL) antioxidant activity and extracted some compounds from mulberry (*Morusalba* L.) leaves. They found that quercetin 3-(6-malonylglucoside) and

rutin are the chief flavonol glycosides in the mulberry leaves. Kim et al., (1999) isolated nine flavonoids from mulberry leaves and examine for free radical scavenging function and confirmed to be antioxidative.

VI. 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) mulberry leaves were reported to having antipyretic and anti-inflammatory effects. According to Chai (2005) flavonoids and related compounds were isolated from *Morusalba* which exhibited the anti-inflammatory effects. They found that extract obtained from the bark of *Morusalba* root in hot water has strong antihistaminic and antiallergic activity.

VII. VASOACTIVE AND NEUROPROTECTIVE ACTION

Vasoactive effects result in either increasing or decreasing blood pressure. According to Xia et al., (2008) ethyl acetate extract from leaves of *Morusalba* 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). Morin, a flavonoids found in mulberry which reduced the tissue level of cyclosporine and act as immunosuppressive agent with narrow therapeutic range and minimize the nitric oxide production by the activated macrophages (Fang et al., 2005). According to Kang et al., (2006) 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 ischemic damage caused by oxygen glucose deprivation (OGD) in PC12 cells. The anaerobic treatment of mulberry leaves makes γ -aminobutyric acid to enhances the neuroprotection effect against in *vivo* cerebral ischemia (Kang et al., 2005).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).

VIII. ANTICANCER ACTION

Many medicinal plants have anti-bacterial, anti-viral, anti-inflammatory, anti-cancer, immunostimilatory and antioxidant properties as well as compounds which effect specific organs.According to Singh et al., (2010) 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) 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 explained its highly useful medicinal properties.

IX. CONCLUSIONS

Mulberry plant is one of the traditional herbs which are 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 explain its medicinal value by Indians.

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Table 1: Active Compounds in mulberry plant

S.N.	Pharmacokinetics actions	Pharmacokinetics principles	References
1	Hypoglycemic activity	Moranolin (DNJ), Moran (glycopeptides), Hydrophobic flavonoids (flavones and flavonone), 2-Arylbenzofuran	Singab, 2005 Fallon, 2008 Singhal et al.,2010
2	Anti obesity action	Ethanolic extract	Oh ,2009
3	Lipid-lowering action	Flavonoids	Li et al .,2005
4	Antioxidants action	Polyphenols, Carotenoids, Vitamins A, C and E, Quercetin 3-(6-malonylglucoside) and Rutin	Andallu ,2001 and 2009 Katesube et al., (2006)
5	Anti-inflammatory actions	Flavonoids	Chai ,2005
6	Antiallergic action	Flavonoids	Chai ,2005
7	Vasoactive action	Ethyl acetate, Morin	Xia et al ., 2008 Fang et al., 2005
8	Neuroprotective action	Cyanidin-3-O-beta-Dglucopyranoside, γ - aminobutyric acid	Kang et al., 2005
9	Anticancer action	Flavanics	Zhang ,2009