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The Effect of *Morus alba*, *Alloe barbadensis* Miller, *Allium sativum*, *Annona squamosa*, and other Medicinal Plants as A Therapeutic Agent for Diabetes Mellitus

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ABSTRACT

This review article discusses the prevalence of diabetes. However, due to the limitations of the traditional medications of diabetes, there is growing interest in using medicinal plants that contain specific chemicals such as alkaloids, terpenoids, carotenoids, flavonoids, and glycosides to combat diabetes. Diabetes mellitus is a chronic metabolic disease that affects millions of people worldwide. The extracts of *Morus alba*, a plant with a long history of traditional use in various cultures, have been shown to possess anti-diabetic properties. This review article summarizes the current research on the use of *M. alba* and various other medicinal plants extracts including *Alloe barbadensis miller*, *Allium sativum*, *Annona squamosa*, *Azadirachta indica*, *Averrhoa bilimbi* as a therapeutic agent for diabetes mellitus. Overall, this review paper provides a comprehensive analysis of the potential of various medicinal plants extracts as a cure for diabetes mellitus and highlights the need for further research to fully evaluate their therapeutic potential.

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INTRODUCTION

The lifestyle and diet changes causing the variation in the metabolism of carbohydrates, proteins, and lipids often leads to a situation of “hyperglycemia” which is commonly known as “Diabetes” (Davis SN, 2006). In general, diabetes is a disease in which a person lacks the ability to synthesis insulin within his/her pancreas. Scientifically, diabetes is characterized as “diabetes mellitus (DM)” and it is a metabolic and chronic type of disease. There are three types of diabetes which include: Type 1 Diabetes, Type 2 Diabetes and gestational diabetes (GDM) (International Diabetes Federation, 2022). The symptoms of diabetes often vary from long term to short

term and from type 1 diabetes to type 2 diabetes. The symptoms include fatigue, sudden weight loss, blurred vision, frequent urination, constant hunger and abnormal thirst. The symptoms of type 2 diabetes include: family history, unhealthy diet, lack of physical activity, increasing age, overweight, high blood pressure, and poor nutrition during pregnancy (International Diabetes Federation, 2022). In 21st century, diabetes is the 5th most leading disease in the world and over 2.8% of the world population is diabetic; this percentage is assumed to raise on approx. 5.4% of the whole world population by the 2025 (Mukesh and Namita, 2013; Kazi, 2014). In the past the 3 decades the medication of diabetes, various

methods are used such as i.e. injecting different types of insulins, metformin, sulfonylureas, healthy diet, and physical exercise. These treatments involve several disadvantages like sulfonylureas lose their effective against the disease after few years and not able to control the state of hyperlipidemia (Dey *et al.*, 2002). In the modern world technology, many treatments against diabetes involve the medicinal plants which contain specific chemicals that act as anti-diabetic. Most of these medicinal plants contain alkaloids, terpenoids, carotenoids, flavonoids, and glycosides (Afrisham *et al.*, 2015). After having a look on the increasing statistics of diabetes patients all around the world, the main ambition of writing this review article is to highlight the use of medicinal plants which are highly effective against diabetes; in order to make the treatment of diabetes more easy and effective.

Diabetes is a worldwide disease mainly characterized by the increase in glucose sugar leading to “hyperglycemia”. Various countries are working on medicinal plants to control and to treat diabetes effectively.

Some of the medicinal plants which are effective against diabetes and are considered as anti-diabetic are listed below.

Effect of *Morus alba* plant against *Diabetes mellitus*

Despite all the advances and modern technology achievements in the medicinal, pharmacological and research fields there are still some methods which are being used as traditionally for the cure, inhibition and prevention of the infections or diseases. Most of the Asian countries have been using medicinal plants traditionally for the treatment of DM; its most specific example is the consumption of Mulberry plant against DM in China from decades (Helin *et al.*, 2018). Different parts of mulberry like leaves, bark, and fruit contain various active compounds which work as therapeutic agent against DM. These active compounds of include flavonoids, polysaccharides and polyhydroxylated alkaloids. The mulberry plant which is scientifically called as *Morus alba* is one of the main specie of the genus *Morus* and belongs to the family Moraceae (Venkatesh and Chauhan, 2013). Scientific research proves that the leaves of *M. alba* can be utilized in different ways and can have different influences including the biological effects as prevention of diabetes, protection of nerve cells, protection against microbes, anti-cancer and anti-inflammatory effects (Butt *et al.*, 2008).

Medicinal Potential of Different Parts of *Morus alba*

Plant

Mulberry leaves: The mulberry leaves powder (MLP) is used for the measuring the antidiabetic effect in STZ-diabetic rats while taking the Glibenclamide as the comparative drug control (Andallu *et al.*, 2012). The study revealed that the MLP have a great effect in reducing the amount of Taxotere or Taxol, carboplatin, and Herceptin (TCH), Triglycerides (TG), Low density lipoprotein cholesterol (LDL-c), very low-density lipoprotein (VLDL), and plasma and urinary peroxides; with a rise in the amount of HDL-cholesterol (Cui *et al.*, 2006). It has also been analyzed by the research studies that the MLP has the ability to produce the anti-oxidative enzymatic effects against DM (Kumar *et al.*, 2010). The liquid extracts of the mulberry leaves are being used as a herbal tea for the treatment of DM as they possess anti-diabetic effects. The liquid extract of the *M. alba* plant are overserved to be significantly rising the glucose levels in the body (Bondada *et al.*, 2014) and produce the inhibitory signal for the enzymes sucrase, maltase and alpha-glucosidase (Chen *et al.*, 1995).

Mulberry branches and twigs: The extract obtained from the bark of branches of the mulberry plant is responsible for the regulation of glycometabolism genes, increase in the expression of Ins 1, Ins 2 genes of the RNA, reduction in the Ins resistance when they're treated against DM (Cui *et al.*, 2006). The extract from the mulberry twigs acts as the organic anti-oxidative agent (Chang *et al.*, 2011) and also inhibits the PTP 1B, thus by producing effectiveness against DM (Liu *et al.*, 2014).

Mulberry root bark: Research studies have proven that the protein tyrosine phosphate 1B (PTP 1B) inhibitor is highly effective against treating DM-type 2 and also obesity. There is a high amount of PTP 1B inhibitor present in the liquid extract of the root bark of the mulberry plant species *Morus spp.* (Yang *et al.*, 2010).

Mulberry Fruit: Freezed fruit of mulberry were utilized for the synthesis of Mulberry fruit powder (MFP). The anti-diabetic effect or the medicinal potential of the MFP is similar to the activity of the MLP; as it reduces the amount of TCH, TG, LDL-cholesterol, VLDL, and plasma peroxides; whereas; increases the of HDL-cholesterol. It is also shown to be responsible for reducing the amount of product of lipid peroxidation process and also thiobarbituric acid-related compounds which are present significantly in liver and Serum and boosts the level of concentration of Superoxide dismutases (SODs) in the Red blood cells (RBCs) and liver with an increase in the concentration of

GSH-Px (Hansawasdi and Kawabata, 2006). Below is the short descriptive table which shows the different types of active compounds which are medicinally effective against

treating DM and are present in various parts of the Mulberry plants.

Table 1. Showing different chemically active compounds present in different parts of Mulberry Plant.

Part of Mulberry Plant	Chemically Active Compound Present
Leaves	Steroids, alkaloids, flavonoids, amino acids, triterpene and some of the organic compounds are present.
Twig	Mostly monosaccharides are present in the twig parts of the Mulberry, i.e. glucose, maltose, fructose, arabinose.
Root Bark	It also contains flavonoids specifically mulberrin and cyclomulberrin.
Fruit	The fruit part contains fatty glycerides like oleic acid and linoleic acid and also some Vitamins B1 and B2.

Chemically active compounds occurring in Mulberry

As we have seen through the table 1 that there are different chemically active compounds in mulberry which are effective against treating DM due to their high

medicinal potential. Although there are some compounds which are mainly occurring in all parts of the plant simultaneously; these are given in the below table.

Table 2. showing the chemical compounds with their activated forms in which these are present in Mulberry Plant.

Chemical Compound	Some of the Activated Form present in Mulberry Plant
Polyhydroxylated Alkaloids	1-deoxynojirimycin (DNJ), fagomine, 3-epifagomine, 2-O- α -D-galactopyranosyl-1-deoxynojirimycins, 6-O- β -D-glucopyranosyl-1-deoxynojirimycins, 4-O- α -D-glucopyranosyl-1-deoxynojirimycins (Kimura <i>et al.</i> , 1995).
Flavonoids	Astragalin (Tao <i>et al.</i> , 2013), quercetin 3-(6-malonylglucoside) (Q3MG) (Katsube <i>et al.</i> , 2010), kaempferol3-(6-malonylglucoside) (K3MG) (Sugiyama <i>et al.</i> , 2013), kuwanon L.
Polysaccharides	Sprague-Dawley (SD)2-3 (Lv <i>et al.</i> , 2007), SD3-3 and SD3-4 (Cui, <i>et al.</i> , 2006)
Others	Moracin M, mulberrofuran C, chlorogenic acid (Zhang <i>et al.</i> , 2007)

Effect of other medicinal plants extracts against Diabetes mellitus

All these plants extracts are used for research on streptozotocin (STZ)-induced diabetic rats.

Allium sativum (Garlic): Ethanolic effects obtained from the garlic are responsible for the significant decrease in the glucose, overall cholesterol, urea and uric acid, ceratinine. While comparing the performance of garlic Ethanolic extracts and the anti-diabetic drug “glibenclamide” showed that the 600mg/kg (used for 14 days) of these plant extract were more effective than glibenclamide (Afrisham *et al.*, 2015). Varying research showed that the juice, Ethanolic extracts, and oil of *Allium sativum* help reduce the blood glucose level by preparing insulin in the cells of pancreas (Eidi *et al.*, 2006).

Alloe barbadensis miller (Aloe vera): *Aloe vera* is traditionally used as a medicinal plant in variety of

diseases. The Ethanolic extracts obtained from the fresh leaf gel behave as anti-diabetic and produce hypoglycemic effect. The 300 and 500mg/kg extracts of these plants used for 42 days are compared with the standard anti-diabetic drugs glibenclamide and metformin (Kazi, 2014).

Aschyranthes aspera (Chaff-flower): The Ethanolic extracts of the *Aschyranthes aspera* (1000 mg/kg) reduces the blood glucose level by indicating the stop sign to the absorption of glucose from the intestinal cells (Shinde *et al.*, 2014).

Andrographis paniculata (Bitter weed): The extracts obtained from the aerial parts of the *Andrographis paniculata* are when treated orally; they significantly lower the blood glucose level and the glucose 6-phosphate working for the liver tasks. More study has showed that the extracts are more effective in reducing

the fasting serum triglyceride by 49.8 % as compared to the anti-diabetic drug metformin which reduces it by 27.7%. Moreover, these Ethanolic extracts are involved in the raise of glucose metabolic activities (Kumar *et al.*, 2011).

***Annona squamosal* (Sugar apple):** The plant extracts obtained from the *Annona squamosal* contain many antioxidant effects. These extracts are used for studying hemoglobin, blood glucose, plasma insulin, glycosylated hemoglobin, anti-oxidant enzyme and lipid peroxidation within the liver and kidney cells by the process of oral treatment for 30 days (Kaleem M, *et al.*, 2006). After 30 days, it has been observed that this plant extracts highly reduced the level of blood glucose, lipids, and lipids peroxides. Although the activity level of plasma insulin and anti-oxidant enzyme is increased. The main function of this extract is to control the diabetes caused by the lipid peroxides and anti-oxidants by regulating the activity levels of lipids, insulin and glucose (Zhang and Tan, 2000).

***Argyreia nervosa* (Silver Morning Glory):** The Ethanolic extracts of *Argyreia nervosa* are obtained from its roots and are responsible for significantly reducing the blood glucose level within the time period of 2 hours. Within 2 hours the glucose level is dropped down from 118.45.4 to 96.44.2 mg/dl (Zhang and Tan, 2000).

***Azadirachta indica* (Neem):** When the extracts of *Azadirachta indica* obtained from its leaves and seed oil are used for 4 weeks; it has been observed that the blood glucose is decreased significantly and the working procedure of these extracts is exactly the same as compared to the anti-diabetic drug glibenclamide (Khosla P, *et al.*, 2000). The extracts of root and bark of neem are when given a single dose they worthy reduce the cholesterol level up to 15%, lipids 15%, triglycerides 32%, urea 13%, glucose 18% and ceratinine 23% (Hashmat I, *et al.*, 2012). The neem extracts are also useful

for the hinder of diabetes.

***Averrhova bilimbi* (Star Fruit Tree):** The effect of extracts of *Averrhova bilimbi* is noticed for 2 weeks by treating with 2 doses per day. The extracts are treated with distilled water and their activity is measured with comparison to metformin. The notable results include that the effect of these extracts causes the reduction in glucose by 50% and triglyceride by 130% but the level of HDL-cholesterol raised by 60%. These extracts also behave as anti-lipid per oxidative and anti-atherogenic (Pushparaj P. *et al.*, 2000).

***Biophytum sensitivum* (Life Plant):** The *Biophytum sensitivum* is highly effective against the diabetes and the use of its extracts for 28 days showed the significant decrease in blood glucose and glycosylated hemoglobin in both normal and diabetic rats by allowing the beta-cells to synthesize insulin (Puri, 2001). The extracts of life plant contain amino acids, terpenes, steroids, saponins, flavonoids, polysaccharides, and pectin. This plants extracts are also characterized for the increase in plasma insulin, liver glycogen, and hemoglobin in the diabetic rats (Pawar and Vyawahare, 2014). Also a significant increase in the activity of glucose 6-phosphate and decrease in the activity of fructose 6-phosphate have been noted through the results of conducted research.

***Barleria prionitis* (Porcupine Flower):** The extracts of the *Barleria prionitis* are responsible for a significant decrease in blood glucose and glycosylated hemoglobin, while increases the level of insulin and liver glycogen (Dheer and Bhatnagar, 2010). These extracts are also responsible for the prevention of weight loss (Geetha and Wahi, 2001).

***Bryonia alba* (Wild Hop):** The extracts of *Bryonia alba* are the evidence in the history that plants can be used against the diabetes. The Ethanolic extracts of this plant are highly effective in reducing the blood glucose in diabetic rats within 7 days (Singh *et al.*, 2012).



Figure 1. Fruiting Branch from a Mulberry Tree (*Morus alba*).



Figure 2. *Allium sativum* (Garlic)



Figure 3. *Alloe barbadensis* plants (*Aloe vera*).



Figure 4. *Aschyranthes aspera* (Chaff-flower)



Figure 5. *Andrographis paniculata* (Bitter weed)



Figure 6. *Annona squamosa* (Sugar apple).



Figure 7. *Argyria nervosa* Bush (Silver Morning Glory).



Figure 8. *Azadirachta indica* Tree (Neem)

Figure 9. *Averrhoa bilimbi* Tree (Star Fruit Tree)Figure 10. *Biophytum sensitivum* Little Tree (Life Plant)Figure 11. *Barleria prionitis* (Porcupine Flower)Figure 12. *Bryonia alba* plant (Wild Hop)

CONCLUSION

This review paper is summarized on the study of different research papers which comprise of the data analytics and records of the medicinal potential of various *Morus alba* and various other plants which have been significantly used in traditional way for treating Diabetes mellitus. The descriptive study of different parts of the mulberry plant and the various active compounds occurring in its different parts is carried out in this review. Although various other botanical species which are responsible for exhibiting the positive effects and which tend to act as anti-diabetic are listed and described.

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CONFLICT OF INTEREST

The authors have not declared any conflict of interests.

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