Antidiabetic activity of bark extract of ficus microcarpa: a Review

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ABSTRACT: Diabetes mellitus is one of the major health problems in the world, the incidence and associated mortality are increasing. Inadequate regulation of the blood sugar imposes serious consequences for health. Conventional antidiabetic drugs are effective, however, also with unavoidable side effects. On the other hand, medicinal plants may act as an alternative source of antidiabetic agents. The present investigation of Ficus microcarpa linn. Stem bark extracts were studied for antidiabetic activity studies. In preliminary phytochemical screening ethanolic extracts showed positive results for saponins compounds, flavonoids, carbohydrates and tannins & Proteins. The blood glucose level was observed in normal group(I) see that of the blood glucose level was 110μg/dl in 14th day. In disease control group (II) blood glucose level was 347μg/dl in 14th day. In standard group (III) showed antidiabetic activity significantly decresed blood glucose level was 67.66μg/dl in 14th day. In aqueous extract treated group (IV) significantly decreased blood glucose level was 86.83μg/dl in 14th day. In ethanolic extract treated group (V) significantly decreased blood glucose level was 74.88μg/dl in 14th day.
KEYWORDS: Ficus microcarpa, bark extract , Antidiabetic activity.

I. INTRODUCTION
1.1 HERBAL MEDICINE
Since time immemorial, mankind has used plant extracts from different plants tocure many diseases and thus relieve him from physical agony [1]. In our country,the traditional system of medicine plays an important role in health care of ruralpeople for all types of ailments. The healing power of traditional herbal medicineshas been realized and documented since Rigveda and Atharvaveda [2]. Since then plants and their extracts have been used therapeutically and even today plant-based medicines continue to play an essential role in world health care [3]. India has about 45,000 plant species and more than 35,000 plant species have been claimed to possess medicinal properties and are being used in various human cultures around the world for medicinal purposes [4]. The term of medicinal plants include a various types of plants used in herbalism and some of these plants have a medicinal activities. Medicinal plants are the "backbone" of traditional medicine, which means more than 3.3 billion people in the less developed countries utilize medicinal plants on a regular basis. These medicinal plants consider as a rich resources of ingredients which can be used in drug development and synthesis. Besides that these plants play a critical role in the development of human cultures around the whole world. The Indian sub-continent has a very rich diversity of plant species in a wide range of ecosystems. There are about 17.000 species of higher plants, of which approximately 8.000 species, are considered medicinal and used by village communities, particularly tribal communities, or in traditional medicinal systems, such as the Ayurveda.

These medicinal plants consider as rich resource of ingredients which can be used in drug development and synthesis. Besides that these plants play a critical role in the development of human cultures around the whole world. Moreover, some plants consider as an important source of nutrition and as a result of that these plants recommended for their therapeutic values. These plants include ginger, green tea, walnuts and some others plants. Other plants their derivatives consider as important source for active ingredients which are used in aspirin and toothpaste.[5]

1.2 DIABETES INTRODUCTION
Diabetes mellitus (DM) consists an enormous public health problem globally, associated with high morbidity and mortality. The disease expected to tak dimensions of an epidemic is often called "the scourge of modern times."Furthermore, the disease involves a variety of implications, such as personal, family, social as

well as high cost for the National Health System for each country due to long hospitalization, diagnostic tests, e.t.c. Diabetes is a disorder characterized by impaired metabolism of carbohydrates, proteins and fats due to inadequate or inefficient activity of insulin. Type II diabetes is characterized by insulin resistance (reduced sensitivity of cells to insulin), a relative insulin deficiency, or both. Type II diabetes usually develops in adulthood, and most patients are obese.

The World Health Organization estimates that the total number of diabetics worldwide will reach 333 million in 2025 from 135 million in 1995.[6,7]Regarding western world Diabetes mellitus is one of the most common chronic since in 2007, it was estimated that there were 246 million people with diabetes compared to 194 million in 2003. This significant increase is expected to take place both in developing and developed countries and is mainly attributed to the modern way of living including sedentary lifestyle, stress and unhealthy nutritional dietary habits. Diabetes is not a disease of contemporary society but it has been recognized since ancient times in the 2nd century BC when the Greek physician Aretaeus from Cappadocia described its' symptoms. From that time onwards, the pathogenesis of diabetes still has not been fully understood and draws a great deal of attention by

the vast majority of literature. Almost three decades ago, maintenance of patients' life was the main therapeutic goal by health professionals, particularly for those suffering from insulin-dependent diabetes. Nowadays, the increase in Diabetics' life expectancy has highlighted the issue of complications such as micro and macro vascular complications (micro and macro-angiopathy). Furthermore, over the last decades much progress in outcome of diabetes mellitus treatment has been within the field of self management and care. Indeed, the reports of patients who lived 40-50 years without some severe complications following "treatment ," indicated that the key-element to confront the disease is the effective management of diabetes[8].

1.2.1Factors contribute in DM
Diabetes involves chronic levels of abnormally high glucose (hyperglycemia). Many patients, especially those with type 2 diabetes, also have elevated blood pressure (hypertension), chronic high levels of insulin (hyperinsulinemia),, unhealthy levels of cholesterol and other blood fats (hyperlipidemia). All of these factors contribute to

the long-term complications of diabetes, which include:

- Vascular disease (diabetic angiopathy), atherosclerosis,heart conditions and stroke: These cardiovascular disorders are the leading cause of death in people with diabetes.
- Kidney disease (diabetic nephropathy): Diabetes is the chief cause of endstage renal disease, which requires treatment with dialysis or a kidney transplant.
- Eye diseases: These include diabetic retinopathy, glaucoma and cataracts. Diabetes is a leading cause of visual impairment and blindness.
- Nerve damage (diabetic neuropathy): This includes peripheral neuropathy, which often causes pain or numbness in the limbs, and autonomic neuropathy, which can impede digestion (gastroparesis) and contribute to sexual dysfunction and incontinence. Neuropathy may also impair hearing and other senses.
- Impaired thinking: Many studies have linked diabetes to increased risk of memory loss, dementia, Alzheimer's disease and other cognitive deficits. Recently some researchers have suggested that Alzheimer's disease might be "type 3 diabetes," involving insulin resistance in the brain.
- Infections and wounds: Foot conditions and skin disorders, such as ulcers, make diabetes the leading cause of nontraumatic foot and leg amputations. People with diabetes are also prone to infections including periodon disease, thrush, urinary tract infections and yeast infections.
- Cancer: Diabetes increases the risk of malignant tumors in the colon, pancreas, liver and several other organs.
- Musculoskeletal disorders: Conditions ranging from gout to osteoporosis to restless legs syndrome to myofascial pain syndrome are more common in diabetic patients than non diabetics.
- Pregnancy complications: Diabetes increases the risk of preeclampsia, miscarriage, stillbirth and birth defects.
- Emotional difficulties: Many but not all of the studies exploring connections between diabetes and mental illness have found increased rates of depression, anxiety and other psychological disorders in diabetic patients. In addition to chronic hyperglycemia, diabetic patients can experience acute episodes of

hyperglycemia as well as hypoglycemia (low glucose). Severe cases can cause seizures, brain damage and a potentially fatal diabetic coma.

- Insulin shock: This advanced stage of hypoglycemia is typically due to excessive amounts of insulin medication or certain antidiabetic agents.
- Diabetic ketoacidosis: A lack of insulin can force the body to burn fats instead of glucose for energy. The result is a toxic byproduct called ketones, along with severe hyperglycemia.
- Hyperosmolar hyperglycemic nonketotic state: This involves severe hyperglycemia and dehydration. These dangerous glucose complications are most common in patients with unstable diabetes, but they can develop even in individuals who do not realize they have diabetes. About one-third of the estimated 20.8 million Americans with diabetes have not yet been diagnosed, according to the U.S. Centers for Disease Control and Prevention (CDCP, 2005).[9]

1.2.2 Complications:
I. Eye complication
The major complication of disease on eye is DIABETIC RETINOPATHY. This causes leakage of the protein and blood in the retina because of a diseased small vessel in the back of the eye. The disease in these blood vessels may also cause the formation of small aneurysms and new but brittle blood vessels. Spontaneous bleeding from these new blood vessel leads to retinal detachment and impair the vision. Cataract or glaucoma are also most common in diabetic patient.

II.Nephritis[10][11]
This is also called as DIABETIC NEPHROPATHY. The onset of kidney damage is varied from patient to patient. Initially diseased blood vessels of the kidney lead to leakage of the protein in the urine. Later on, the kidney loses its ability to cleanse and filter the blood which leads to the accumulation of toxic waste products in the kidney.

III. Paralysis[12][13]
The nerve damage from the diabetes is called as DIABETIC NEUROPATHY. It is also caused by micro vascular disease. In this disease most essentially blood flow to the nerves is decreased, and leave the nerve without blood as a result the nerves get damaged. Symptoms of the diabetic nerve damage are numbness, burning and aching of the feet and lower extremities. When the diabetic neuropathy causes the complete loss of sensation to the feet, patient may not be aware of the injury to the feet. Diabetic neuropathy also causes the erectile dysfunction by affecting the nerve which is important for penile erection. Diabetic neuropathy may also nausea, diarrhea, weight loss and other gastro paresis by affecting the nerve of the stomach and intestine.[14]

The complications are related to the disease of blood vessel which is classified: Micro Vascular Disease:-A small vessel disease which involves eye, kidney and nerves. Macro Vascular Disease:- A large vessel disease which involves heart and blood vessels. Diabetes may also lead to atherosclerosis (hardening of arteries) of large blood vessels, which leads to angina, stroke and pain in lower extremities.[15][16]

1.2.3 Causes Of Diabetes
The causes of diabetes are complex and only partly understood. This disease is generally considered multi-factorial, involving several predisposing conditions and risk factors. In many cases, genetics, habits and environment may all contribute to a person's diabetes. To complicate matters, there can be contrary risk factors for the various forms of the disease. For example, autoimmune diabetes (type 1 and latent autoimmune diabetes of adulthood, LADA) is more common in white people, but metabolic diabetes (type 2 and gestational diabetes) is more common in people of other races and ethnicities. Type 1 is usually diagnosed in children, but advancing age is a risk factor for type 2 and gestational diabetes. Insulin resistance, prediabetes and metabolic syndrome are strong risk factors for type 2 diabetes. Other diabetic risk factors and causes include:

i. **Genetics And Family History:-**Certain genes are known to cause maturityonset diabetes of the young (MODY) and Wolfram syndrome. Genes also contribute to other forms of diabetes, including types 1 and 2.

ii. **Family Medical History Is Also Influential To Varying Degrees:-** For example, a person whose parents both have type 1 diabetes has a 10 to 25% chance of developing that disease, according to the American Diabetes Association, and someone whose parents both have type 2

diabetes has a 50% chance of developing that disease.

iii. **Weight And Body Type**:-Overweight and obesity are leading factors in type 2 diabetes and gestational diabetes. Excess fat, especially around the abdomen (central obesity), promotes insulin resistance and metabolic syndrome. Most people with autoimmune diabetes (type 1 and LADA) are of normal weight, and excess weight has not traditionally been considered to be related to these conditions. However, recent research indicates that obesity may hasten the development of type 1 diabetes and that the increasing rate of type 1 diabetes may be at least partly due to the rise of childhood obesity. Furthermore, patients with autoimmune diabetes who gain weight are susceptible to insulin resistance and double diabetes.

iv. **Sex:-** Though men make up less than 49% of the U.S. adult population, they account for 53% of the adult cases of diabetes, according to the National Institutes of Health (NIH). The prevalence of diabetes in American men and women was similar until 1999, when a growing disparity began, according to an analysis of statistics published by the U.S. Centers for Disease Control and Prevention (CDC). Little or no research has been conducted to explain this trend. One factor may be the documented increase in recent years of low testosterone levels (male hypogonadism), which scientists have linked to insulin resistance.

v. **Level Of Physical Activity:-**Lack of regular exercise is blamed for much of the twin global epidemics of obesity and diabetes.

vi. **Diet:-**The effect of diet in the development of diabetes is controversial. Some studies have linked heavy consumption of soft drinks and other simple carbohydrates to risk of metabolic diabetes, and foods low in the glycemic index, such as whole grains, to reduced risk. Yet the ADA states that eating foods containing sugar does not cause the disease. The culprit, rather, is the weight gain due to sedentary habits and excess intake of calories, according to the ADA. Another dispute centers around whether being fed cow's milk early in life might be linked to type 1 diabetes. Some researchers have noted a connection, but

others have not. Further scientific research is likely on this topic.

vii. **Other Diseases:-**Medical conditions including high blood pressure, hyperlipidemia (unhealthy levels of cholesterol), polycystic ovarian syndrome, asthma and sleep apnea have been linked to type 2 diabetes. Celiac disease (gluten intolerance) and other autoimmune diseases have been linked to type 1. The many conditions that may cause secondary diabetes include pancreatitis, hemochromatosis, endocrine disorders including hyperthyroidism, Cushing's disease and acromegaly, and genetic conditions including cystic fibrosis, Down syndrome and some forms of muscular dystrophy, Diabetic foot and urinary tract infection.

viii. Hormones:-These chemical messengers can contribute to diabetes in various ways. For example, stress hormones such as cortisol have been linked to fluctuating glucose levels in type 2 diabetes, and stress hormones in women during pregnancy have been linked to risk of type 1 diabetes in the child. The release of growth and sex hormones during adolescence may make some teens anabolic steroids, growth hormone, estrogens, injected contraceptives, androgen deprivation therapy for prostate cancer and corticosteroids have been linked to secondary diabetes.

ix. **Medical Treatments:-**In addition to hormonal therapies, medications including diuretics, beta blockers (another class of antihypertensives), immune suppressives, antiretrovirals (AIDS/HIV drugs) antipsychotics, lithium, and some antidepressants, anticonvulsants and chemotherapy drugs have been linked to an increased risk of secondary diabetes. Pancreatectomy and radiation therapy may also result in secondary diabetes. Drugs including pentamidine (used to treat pneumonia) and L–asparaginase (used to treat leukemia) have been linked to type1 diabetes.

x. Other chemicals:-In addition to these pharmaceuticals, some studies have linked PCBs, other pollutants and certain pesticides including the defoliant Agent Orange and dioxin (its active ingredient) to insulin resistance and type 2 diabetes.

Common consumer plastics and plastics ingredients including phthalates and bisphenol A have also been linked to insulin resistance in some cases. Exposure to agricultural pesticides during pregnancy has been tentatively linked to gestational diabetes. A rat poison called pyriminal has been linked to type 1 diabetes.

xi. **Other environmental factors:-** Some researchers theorize that free radicals may contribute to the development of type 1 and possibly other forms of diabetes. Free radicals are formed as a result of chemical reactions in the body. Smoke, air pollution and even genetics contribute to the formation of free radicals. When these radicals build up, they can destroy cells, including those involved in the production of insulin.

xii. **Viruses:-**Some people are diagnosed with type 1 diabetes after a viral infection. Viruses thought to be related to type 1 diabetes include mumps, rubella and coxsackie virus (related to the virus family that causes polio and hepatitis).

xiii. **Smoking:-**Cigarette smoking is a risk factor for type 2 diabetes and possibly other forms of diabetes.

xiv. **Alcohol:-**Excessive use of alcohol is a risk factor for diabetes. For example, it can cause pancreatitis.[17]

1.3 FICUS MICROCARPA LINN.

Ficus microcarpa, also known as Chinese banyan, Malayan banyan, Indian laurel, curtain fig, or gajumaru is a tree in the fig family Moraceae. It is native in a range from China through tropical Asia and the Caroline Islands to Australia.[18-20] It is widely planted as a shade tree[21] and frequently misidentified as F. retusa or as F. nitida (F. benjamina).[22]

Large or medium-sized, evergreen, glabrous tree with a dense crown, Bark dark grey, Leaves elliptic, ovate or obovate, rounded or bluntly acuminate, polished, glossy; nerves not prominent. Receptacles about 6-3 x 6-9 mm., sessile, paired, depressed-globose, smooth, yellowish-reddish, subtended by 3, persistent bracts. Flowering & fruiting: March – October.

Dyes: - Light Pink dye found in bark of the tree. Alum used as a Mordant for coloring of cotton cloth[23] Bark of Ficus microcarpa is used in wounds, ulcers, bruises, diarrhea, dysentery and leucorrhoea. Its aerial roots are used to treat dental caries[24]

It is an evergreen tree, full grown to highest of 15 m (50 ft) or more, with a rounded dense crown, smooth gray bark, milky sap, and long, thin, dangling aerial roots. Leaves alternate, simple, leathery, deep glossy green, oval-elliptic to diamondshaped, 13 cm (5 in) long, with short pointed, ridged tips. Flowers tiny, unisexual, numerous, hidden within the "fig," a fleshy, specialized receptacle that develops into a multiple fruit (syco-nium), this green turning to yellow or dark red when ripe, sessile, in pair sat leaf axils, small, to 1 cm (0.5 in) in diameter.
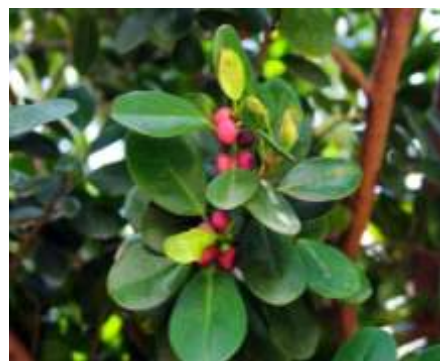

Fig.No.-01 Plant Of Ficusmicrocarpa.

1.3.1.Plant Profile
- **Botanical Name:- Ficus microcarpa**
- **Family :- Moraceae**
- **Scientific classification:-**

1.3.2. Part used of plant
- Leaves: The leaves are pale green, fruity in young in odor, taste in bitter, oblong shape, 8.0 to14.2 cm in length, 4 to 5 cm in width in size, glabrous in surface characteristics.
- Root: The root is light brown, fruity odor, taste in bitter, cylindrical shape, and rough irregularly cracked in surface characteristics.
- Bark: The barks are grey to dark brown, fruity in odor, taste in bitter, cylindrical shape, and rougher regularly cracked bark in surface characteristics.[25]
- Fruit: Fruits are small and turn from pink to purple when ripe.

- Flowers: Flowers are tiny, unisexual and borne within a round structure called the syconium or fig.[26]

1.3.3 Microscopic Characters

- Leaves: The transverse section of leaf showed palisade, epidermis, spongy mesophyll, phloem, xylem and abaxial surface.

- Root: The transverse section of root shows, vascular bundles, medullary rays, calcium oxalate crystal, cortex region and pith and powdered sample of root of Ficus microcarpa showed Trichomes, Starch grain, Lignified cell, fibres and oil globules.

- Bark: The transverse section of barks show fibers showing thick cells of the parenchymatous cells, cork cells, cortex, pigment, vascular bundles and starch grain

1.3.3. Distribution:-It is well distributed in forests at low and medium altitudes ascending to 1,500 meters. It occurs throughout India, southern China, and Taiwan. In India, it is found in chota Nagpur, Bihar, Central India[27]

1.3.4. Chemical composition:-

- Sterols
- Terpenoids
- Glycoside
- Polyphenols
- Carbohydrates
- Maermesin
- Calechin
- Ficuisoflavone
- Isolupinisoflavone E
- Catechol
- Chlorogenic acid
- Methoxybenzoate

1.3.5. Medicinal properties and uses:-The aerial roots used to treat dental caries and odontalgia. The bark and leaves are astringent, refrigerant, acrid and stomachic. They are useful in wounds, ulcers, bruises, flatulent colic, diarrhea, dysentery, diabetes, hyperdipsia, burning sensation, haemorrhages, ulcerative colitis, leucorrhoea,

psychopathy and hepatopathy. The bark is given in buttermilk to cure liver diseases for seven days.[28]

1.4 DISCUSSION
Diabetes mellitus is major manifestation include disordered metabolism and inappropriate hyperglycemia. It is thought that the many stresses inherent in the modern lifestyle may cause an increased incident of diseases such as cancer, heart diseases and hypertension. The rising incidence of such diseases is alarming and becoming serious public health problem. Diabetes one such disease and it is estimated that the number of diabetes patients will continue to increase in future. The species of genus Ficus have the most potent hypoglycemic effects. The majority of the experiments confirmed the benefits of medicinal plants with hypoglycemic effects in the management of diabetes mellitus. Numerous mechanisms have been proposed for these plant extracts. All of these actions may be responsible for the reduction of diabetic complications. We believe that these plants may play vital role in future studies on determining the mechanism of their hypoglycemic activity, as well as for the isolation and identification of active hypoglycemic substances. In addition, further comprehensive pharmacological investigations will be carried out to assess the likely toxicological effects of these anti diabetic plants. It is therefore believed that not only should the present study be continued but a rigorous investigation undertaken by plant traditionally used in diabetes for their potential usefulness as an adjunct to conventional therapy

1.5 CONCLUSION
In conclusion, it may be stated that Diabetes is an important human ailment afflicting many from various walks of life in different countries, especially in the urban areas of under develop countries. In last few years there has been an exponential growth in the field of herbal medicines to cure various diseases including diabetes. In this regard the species of genus Ficus are the potential natural source to cure a global problem, Diabetes. There occur a selective decrease in the hyperglycemic state after the administration of extracts of different parts of the species of Ficus, which may be mediated through a number of bioactive compounds present in the extract and these drugs gaining popularity both in developing and developed countries because of their natural origin, lesser side effects and low cost.

It is suggested and assumed that a further exploration of the present research work is needed to come up with an active antidiabetic agent.

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