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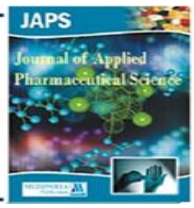

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Hypoglycemic potential of genus *Ficus* L.: A review of ten years of Plant Based Medicine used to cure Diabetes (2000-2010)

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ABSTRACT

Medicinal plants play an important role in cure of Diabetes mellitus all over the world. The aim of this paper is compile data to investigate the effects of plant extract, compounds and active constituents against diabetes. The present review is therefore, an effort to give specifically literature on the pharmaceutically important species of genus *Ficus* L. (Moraceae) with anti diabetic properties, reported in the literature from 2000-2010. Our literature survey showed that there is no comprehensive and systematic data on genus *Ficus* with particularly emphasis on antidiabetic potential based on clinical trials is published elsewhere. There are about 850 species of genus *Ficus* worldwide and among them only 6 species reported to use against diabetes. The profile presented includes its methodology used and their bioactive agents with anti diabetic activity. The species of genus ficus include: *Ficus bengalensis* L., *Ficus carica* L., *Ficus racemosa* L., *Ficus hispida* L. f., *Ficus microcarpa* L.f., *and Ficus religiosa* L. Among these, *Ficus microcarpa* L. f., and *Ficus hispida* L.f., are incorporated first time in this review to be used against diabetes by using experimental animals. Based on biochemical and histological findings, it can be concluded that these plants may develop the healing action of diabetic complications and reflected anti diabetic potential through its glucose lowering activity in alloxan or streptozotocin induced diabetic laboratory animals.

Key words: *Ficus*, Diabetes mellitus, Hypoglycemic, Hyperglycemic, Blood glucose.

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INTRODUCTION

Diabetes is any disorder characterized by excessive urine excretion. The most common form of diabetes is Diabetes mellitus, a chronic, progressive, systematic condition of impaired carbohydrate metabolism (Sachan et al., 2009). Diabetes is the world's largest endocrine disease associated with increased morbidity and mortality rate (Sophia and Manoharan, 2007). Diabetes mellitus is also associated with long term complications including retinopathy, nephropathy, neuropathy and angiopathy and several others (Sharma et al., 2010). According to International Diabetes Federation(IDF) in 2007, 246 million people worldwide affected by diabetes mellitus and making the disease one of most non-communicable global disease and fourth leading cause of death in world. Plants are always an exemplary source of drugs infact many of the currently available drugs were derived either directly or indirectly from them (Arayne et al., 2007). A variety of ingredients present in medicinal plants are thought to act on a variety of targets by various modes and mechanisms. They have potential to impart therapeutic effect in complicated disorders like diabetes and its complications (Tiwari and Rao, 2002).

The current interests in natural therapies and traditional medicines have motivated the investigation into plants that have traditionally been used in relation to diabetes (Perez et al., 2003). More than a quarter of the medicines in use today come from plants, i.e. from traditional medicine (Serraclara et al., 1998). According to world ethnobotanical information reports, almost 800 plants may possess antidiabetic potential (Alarcon-Aguilara et al., 1998). Several species of genus *Ficus* (family: Moraceae) are being used traditionally in a wide variety of ethno medical remedies (Ahmed and Urooj, 2009).

Present review is focused on experimental studies by using different parts including bark aerial roots, leaves, fruits and roots of *Ficus* species and their bioactive components against diabetes. This review includes antidiabetic effects of *Ficus* species with particular emphasis on In vivo experiments by using laboratory animals. This study will lead to discover more scientific knowledge about the diabetes; a global problem for developed, developing and under developed countries.

***Ficus bengalensis* L.**

Aqueous extract of aerial roots

The dose of 300 mg/kg of aqueous extract of *Ficus bengalensis* aerial roots effect on blood glucose level of normal-, sub- and mild-diabetic rats have been studied and the results were showed the maximum fall of 43.8 and 40.7% in blood glucose leveling normal rats, respectively. The same dose showed the marked reduction in blood glucose level of 54.3% in sub- and 51.7% in mild-diabetic rats during glucose tolerance test. The concentration of Mg(1.02%) and Ca (0.85%) identified through laser induced breakdown spectroscopy in the most effective dose could be responsible for this high percentage fall in blood glucose level as they take part in glucose metabolism (Singh et al., 2009).

Ethanolic extract of fruit, bark and aerial roots

Oral administration of ethanolic extracts of the fruit, aerial root and bark of *Ficus bengalensis* for 21 days produced significant decrease in blood glucose, i.e., decreases of 31.73, 18.33 and 28.84% respectively. Oral administration of glibenclamide 0.5 mg/kg showed the maximum reduction 34.4% in blood glucose level. The ethanolic extract of the fruit, at the dose of 120mg/kg body weight was found to exert a more pronounced antidiabetic activity than the other morphological parts of the same plant. The alcoholic extracts of aerial roots and bark also brought down the blood glucose level, though not as much as the extract of fruit (Sharma et al., 2007).

***Ficus carica* L.**

Aqueous extract of leaves

To investigate the hypoglycaemic activity of *Ficus carica* leaf aqueous extract, a decoction was administered to rats in lieu of drinking water for three weeks. The groups were: untreated non-diabetic, untreated diabetic, treated non-diabetic and treated diabetic animals. The extract decreased plasma glucose in diabetic while not in normal rats. Plasma insulin levels were decreased by treatment in non-diabetic rats by the action of anti diabetic phytochemicals as given in Table.1. Thus, *Ficus carica* extract showed a clear hypoglycemic effect in diabetic rats (Perez et al., 2000).

Leaves fed in basal diet

There was a drastic reduction in blood glucose level in all tested groups which fed on basal diet containing different levels of *Ficus carica* L. as compared to the control positive group. Feeding diabetic group basal diet containing 10 and 20% of ficus carica L. The highest reduction in blood sugar was achieved by feeding high level of *Ficus carica* L. *Ficus carica* L. leaves showed greatest significant decrease in serum glucose level which was achieved by 8% (El-shobaki et al., 2010).

Organic extract of leaves

The antidiabetic effects of *Ficus carica* leaf extracts have been reported previously. From the aqueous decoction of fig leaves, after treatment with HCI, centrifuging, treatment with sodium hydroxide (NaOH) and extraction with chloroform (CHCl3), the administration of the organic phase rats with streptozotocin-induced diabetes led to a decline in the levels of total cholesterol and an decrease in the total cholesterol/HDL cholesterol ratio (with respect to the control group), together with a reduction of the hyperglycemia (Canal et al., 2000).

Aqueous and chloroform extract of leaves

Streptozotocin induced diabetic rats divided into groups one of them received a single dose of basic fraction of *Ficus carica* extract and another received a single dose of chloroform fraction of the extract interaperitonially. The results showed that the aqueous (basic) and organic (chloroform) extracts of *Ficus carica* leaves have similar effects in reducing hyperglycemia in diabetic rats, whereas the chloroform extract has a greater effect in reducing fatty acid level too (Perez et al.,2002).

***Ficus hispida* L. f**

Ethanolic extract of bark

Albino rats were divided into groups receiving different treatments consisting of vehicle, water-soluble portion of the ethanol extract of *Ficus hispida* bark (FH) (1.25 g/kg) and standard antidiabetic drugs, glibenclamide (0.5 mg/kg) and 0.24 units of insulin (0.62 ml of 0.40 units/ml). Blood glucose was estimated in both normal and alloxan-induced diabetic rats before and 2 h after the administration of drugs. To find out the probable mechanism of action of FH as a hypoglycemic agent, i) the glycogen content of the liver, skeletal muscle and cardiac muscle, and ii) glucose uptake by isolated rat hemi-diaphragm were estimated. FH showed significant reduction of blood glucose level both in the normal and diabetic rats. However, the reduction in the blood glucose level was less than that of the standard drug, glibenclamide. FH also increased the uptake of glucose by rat hemi-diaphragm significantly. As the following phyto-constituents involve in control the hyperglycemia given in Table.1 There was a significant

increase in the glycogen content of the liver, skeletal muscle and cardiac muscle. Increased glycogenesis and enhanced peripheral uptake of glucose are the probable mechanisms involved in its hypoglycemic activity (Ghosh et al., 2004).

***Ficus microcarpa* L.f., *(*syn. *Ficus retusa* L.)**

Ethanolic extract of leaves

The ethanolic extract of *Ficus microcarpa* L. leaves (EEFML) was evaluated for its hypoglycemic activity against alloxan-induced diabetic rats. EEFML was administered at 100 and 200 mg/kg body weight orally for 14 days. The blood glucose was estimated on 0, 7 and 15 days treatment. Glibenclamide serve as positive control. Administration of 200 mg/kg of EEFML significantly reduced the amount of blood glucose when compared to diabetic control. These results reveal the beneficial role of *Ficus microcarpa* leaves as potential hypoglycemic agent against alloxan-induced diabetes mellitus in rats, given in Table.1, which may be attributed to the increased levels of antioxidant enzymes and also by preserving the pancreatic ß-cells integrity as evidenced by histopathological studies (Kumar et al., 2007).

Aqueous and *methanolic extract of leaves*

Hypoglycemic activity of the water and methanolic extract *Ficus retusa* leaves obtained through the Microwave Assisted Extraction was evaluated in normal, alloxan-induced diabetic and hyperglycemic normal rats for the 30 days of chronic administration. Overall results showed that both water and methanolic extract *Ficus retusa* leaves at the dose of 200mg/kg possess marked hypoglycemic activity (when tested in fasted normoglycemic rats) and antihyperglycemic activity (by improving the glucose tolerance test and lowering the blood glucose levels in alloxan monohydrate induced rats). Further, hypoglycemic potential of water and methanolic extract were compared with that of standard drug (tolbutamide). In glucose tolerance test, water and methanolic extract (at the dose of 200mg/kg) and tolbutamide lowered the external glucose level in a same manner. Only methanolic extract, was selected for alloxan monohydrate induced diabetic rats a dose of (140mg/kg) and found significant reduction in the blood glucose level of diabetic. The results suggest that the *Ficus retusa* leaves methanolic extract has insulinomimatic activity. The single dose of methanolic extracts (2000mg/kg) of *Ficus retusa* showed antihyperglycemic effect in diabetic rats. From the study, it was observed that *Ficus retusa* extracts were free of undesirable side effects even after chronic treatment upto 14 days (Parial et al., 2010).

***Ficus religiosa* L.**

Aqueous extract of bark

Ficus religiosa is prescribed for the treatment of diabetes mellitus. In the present study, the antidiabetic effect of aqueous extract of *Ficus religiosa* bark (FRAE) was investigated in normal, glucose-loaded hyperglycemic and streptozotocin (STZ)-induced diabetic rats. Oral administration of FRAE at the doses of 25, 50 and 100 mg/kg was studied in normal, glucose-loaded and STZ-diabetic rats. The freshly prepared solutions were orally administered daily for 21 days. The three doses caused significant reduction in blood glucose levels in all the models due to the phyto-costituents given in Table.1. The effect was more pronounced in 50 and 100 mg/kg than 25 mg/kg. FRAE also showed significant increase in serum insulin, body weight and glycogen content in liver and skeletal muscle of STZ-induced diabetic rats while there was significant reduction in the -levels of serum triglyceride and total cholesterol. FRAE also showed significant anti lipidperoxidative effect in the pancreas of STZ-induced diabetic rats. The results indicate that aqueous extract of *Ficus religiosa* bark possesses significant antidiabetic activity (Pandit et al., 2010).

***Ficus racemosa* L. (syn. *Ficus glomerata* Roxb.)**

Methanolic extract of bark

The powdered bark of *Ficus racemosa* was extracted with 90% methanol. The methanolic extract of bark of *Ficus racemosa* demonstrated a significant hypoglycemic effect in alloxan-induced diabetic rats at 3 h after drug administration because of the phytochemicals given in Table 1 and the activity was prolonged upto 24 h. The MEBFR at 200mg/kg dose produced significant activity with a 19.82% reduction in glucose level. Whereas, the maximum antidiabetic activity of 40.33% reduction in glucose level was observed at 24 h after drug administration in the group of animals administrated with 400 mg/kg dose. (Rao et al., 2002).

Aqueous and ethanolic extract of leaves

The hypoglycemic effects produced by the aqueous and ethanolic extracts of *Ficus racemosa* in normal and diabetic induced rats. Oral administration of *Ficus racemosa* extract 400 mg/kg, showed the significant decrease in the glucose level at the end of study after 21 days as compared to the aqueous extract of ficus racemosa (Sachan et al., 2009).

Aqueous extract of bark

Administration of *Ficus racemosa* bark powder (FRP) and *Ficus racemosa* aqueous extract (FRAE) caused a significant reduction of fasting blood glucose level about 54 and 66% respectively in streptozotocin induced rats. The antihyperglycemic effect of FRP and FRAE did not differ statistically with being comparable to that of standard drug that of glibenclamide (Ahmed and Urooj, 2009).

Ethanolic extract of bark

Ficus racemosa ethanolic bark extract were assessed to find out the effective antidiabetic dose in alloxan induced diabetic rats. A dose of 300 mg/kg .b.w FrEBet brought about significant reduction in fasting glucose and urine sugar after 45 days of treatment as compare to that of the dose of 100 and 200 mg/kg. A higher dose of 400 and 500 mg/kg FrEBet had more or less same effect as that of 300 mg/kg (Sophia and Manoharan, 2007).

Ethanolic extract of leaves

Ethanolic extract of Ficus glomerata leaves was subjected to an antidiabetic activity in rats where alloxan monohydrate used as the diabetogenic agent. A marked rise in diabetic control

Table 1: Antidiabetic phyto-chemicals of *Ficus* species

S. No	Name of Species	Part Used	Antidiabetic Phyto-chemicals	References
01.	*Ficus bengalensis* L.	Aerial roots and bark	Mg and Ca methyl ether of leucoanthocyanidin , methyl ethers of leucoanthocyanins, 20-tetra triaconten-2-one , pentatriacontan-5-one , 6-heptatriaconten-10-one , β-sitosterol-α-D-glucoside , meso-inositol	Singh *et al*. 2009. Rastogi and Mehrotra 1979; Subramanian and Misra, 1978.
02.	*Ficus hispida* L.	Bark	Dimethoxy derivatives of leucocyanidin 3-O-b-D-galactosyl cellobioside and Pelargonidin 3-O-a-L-rhmnoside.	Ghosh *et al*., 2004.
03.	*Ficus retusa* L.	Leaf	phenolic constituents (like flavonoids, coumarin and triterpenoids)	Parial *et al.*, 2010.
04	*Ficus religiosa* L.	Bark	β-sitisteryl-D-glucoside	Ambike and Rao, 1967.
05.	*Ficus racemosa* L.	Bark	Leucocyanidin-3-O-β -D-glucopyrancoside, leucopelargonidin-3-O- β -D-glucopyrancoside, leucopelargonidin-3-O-ά-L-rhamnopyranoside. Steroids,alkaloids and tannins. Glycosides, 8-sitosterol, lupeol tannins and psoralens.	Joy *et al.*, 2001. Rao *et al*., 2002. Sophia and Manoharan, 2007.
06.	*Ficus carica* L.	Leaf	Polyphenols and Flavonoids. β-setosterols	El-shobaki *et al.*, 2010. Vaya and Mahmood, 2006.

compares to normal control rats. Ethanolic extract of Ficus glomerata leaves at dose of 250 and 500 mg/kg exhibited o dose significant anti hyperglycemic activity on 4^{th}, 7^{th} and 10^{th} day post treatment. The extract dose of 100 mg/kg also caused reduction in blood glucose level but the results were found statistically insignificant. The antihyperglycemic effect of ethanol extract was found less effective than the reference standard, glibenclamide (Sharma et al., 2010).

Polyherbal alcoholic extract

The polyherbal formulation was prepared by leaves of Syzygium cumini, bark of Ficus glomerata and flowers of Butea superba were extracted in alcohol. Alloxan induced diabetic rats were given 500 mg/kg b.w aqueous solution of polyherbal formulation at the interval of 3, 5 and 7 h. results indicate that polyherbal formulation showed more significant antidiabetic activity in acute as well as prolonged treatment with minimal toxicity (Karigar and Shariff, 2009).

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 (Sachan et al., 2009). 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 (Bnouham et al., 2006).

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 (Aryne et al., 2007). It is therefore believed that not only should the present study be continued but a rigorous investigation undertaken by numerous plants traditionally used in diabetes for their potential usefulness as an adjunct to conventional therapy (Serraclara et al., 1997).

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 (Moraceae) 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 recommended that the plant extract of *Ficus* species can be successfully utilized for the cure of diabetes and related diseases due to their hypoglycemic action.

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