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Anti-diabetic potential of *Ficus racemosa*: current state and prospect especially in the developing countries

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ABSTRACT

As about 50% of the Bangladeshi population is at risk of diabetes each year, the majority of people, especially in rural areas, use herbal medicine alone or alongside prescription drugs for diabetes management. Out of a large number of herbal drugs stated to possess anti-diabetic activity in the Ayurvedic system of medicine, Ficus racemosa is being widely used by the traditional practitioners in the prevention and treatment of diabetes over many centuries in Bangladesh. The fruit, bark, latex, seeds or leaves of F. racemosa plant have been reported to decrease blood glucose levels and improve body weight in diabetic animals when administered in different pharmaceutical preparations and is, therefore, imperative to further investigation. The present review summarize data about phytochemical properties and biological activities of F. racemosa plants and provide scientific evidence for further development and utilization as a potential anti-diabetic drug.

Key words: *Ficus racemosa, physical properties, biological activities, Anti-diabetic potential and developing countries*

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I. Introduction

Plants are an exemplary source of drugs; in fact many of the currently available drugs were derived either directly or indirectly from them. Research on herbal medicines is encouraged to come up with alternative for treatment of diabetes since plant drugs and formulations are considered to be less toxic and free from side effects than synthetic ones (Mitra *et al.,* 1996). In the search for new hypoglycemic compounds, it would be imprudent to ignore the traditional treatment of diabetes, which continues to provide the mainstay of therapy in region of the world where conventional drugs are not readily available or cannot be afforded. According to world ethno-botanical information reports, almost 800 plants may possess anti-diabetic potential (Alarcon-Aguilara *et al.,* 1998). Among them, *Ficus racemosa* is one of the herbs, mentioned in all ancient scriptures of Ayurveda, Siddha, Unani and Homeopathy. All parts of *F. racemosa* plant (leaves, fruits, bark, latex and sap of the root) are medicinally important in the traditional system of medicine in India (Ramana *et al.,* 2011). A wide collection of plant-derived active principles representing numerous bioactive compounds has established its role for possible use

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in the treatment of diabetes (Rizvi and Mishra, 2013). The present review on *Ficus racemosa*, is aiming to draw attention of the researchers to expand the use of this plant in the ethno-pharmacotherapy and the development of new herbal drugs; as the technology is now extremely more powerful than before.

II. Materials and Methods

Plant description

Ficus racemosa Linn. (Family: *Moraceae*), which is considered sacred, has golden coloured exudates and black bark (Joy *et al.,* 2001). This is native to Australia, South-East Asia and the Indian subcontinent. The plant is frequently found around the water streams and is also cultivated (Joseph and Raj, 2010). It is a large deciduous tree up to 18m high, leaves are ovate, ovate-lanceolate or elliptic, sub-acute, entire and petiolate and are shed usually by December and replenished by January and April, when the tree becomes bare for a short period. It has evergreen leaves; if it is close to a water source (Paarakh, 2009). Figs are subglobose or pyriform, red when ripe, borne in large clusters, on short, leafless branches emerging from the trunk and the main branches (Cooke, 1967). The tree is without aerial roots unlike its many family members (Anita and Mittal, 2011).

Scientific classification:

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Rosales
Family : Moraceae
Genus : Ficus
Species : *Ficus racemosa*
Synonyms : *Ficus glomerata* Roxb.
Common names: Jagadumur, Gulangdumur, Yajnadumbar, Udumbara, Gular fig, Cluster fig, Indian fig, Country fig, Goolar Fig, Atti etc.

Table 01. Phyto-chemicals present in the *Ficus racemosa* plant

Sl no.	Plant part	Identified active constituent(s) with references
1	Stem bark	Leucocyanidin-3-O-β-D-glucopyrancoside, leucopelarogonidin-3-O-α-L-rhamnopyranoside, leucopelargonidin-3-O-β-D-glucopyranoside, unidentified long chain ketone, cerylbehenate, lupeol acetate (Paarakh, 2009); β-sitosterol (Joy *et al.,* 2001); lupeol (Joseph and Raj, 2010); α-amyrin acetate (Warrier, 1996); glauanol acetate (Babu *et al.,* 2010)
2	Trunk bark	Lupeol, β-sitosterol (Paarakh, 2009); stigmasterol (Chopra *et al.,* 1958)
3	Root bark	Glycosides, β-sitosterol, lupeol, tannins, psoralens (Gul-e-Rana *et al.,* 2013; Sophia and Manoharan, 2007)
4	Fruit	Glauanol, hentriacontane, β-sitosterol, gluanol acetate, esters of taraxasterol, lupeol acetate, friedelin (Babu *et al.,* 2010); glucose, tiglic acid (Chopra *et al.,* 1992); higher hydrocarbons, other phytosterol (Paarakh, 2009); tannins, gums, steroids, flavonoids, alkaloids (Zulfiker *et al.,* 2011)
5	Leaves	Alkaloids, glycosides, flavonoids, phenolic compound, tannins (Patil *et al.,* 2010); sterols, triterpenoids (lanosterol), tetracyclic triterpene, glauanol acetate (13α, 14β, 17 βH, 20 αH-lanosta-8, 22-diene-3 β-acetate) (Paarakh, 2009); racemosic acid (Kirtikar and Basu, 1998)
6	Latex	Aspartic protease (Paarakh, 2009)
7	Root	Flavanoids (Ghada *et al.,* 2008); tannins (Dreosti, 2000); saponins (Raju and Balaraman, 2008); alkaloids (Punitha *et al.,* 2005); carbohydrates, steroids (Varma *et al.,* 2009)

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Table 02. Phyto-chemicals and their anti-diabetic principles

Sl no.	Phyto-chemicals	Anti-diabetic principles with references
1	Alkaloids	Well known for their anti-diabetic activities by different mechanisms (Varma *et al.,* 2009)
2	β-sitosterol	Have potential anti-diabetic activities (Alam *et al.,* 2012)
3	Flavonoids	Flavonoids are known to regenerate the damaged pancreatic β-cells in diabetic animals (Chakravarthy *et al.,* 1982); Well known for their anti-diabetic activities by different mechanisms (Varma *et al.,* 2009); Have anti-oxidant and free radical scavenging properties that might be responsible for the anti-diabetic activity (Heroor *et al.,* 2013); Known to possess anti-diabetic activity (Vivek *et al.,* 2010)
4	Leucocyanidin-3-O-β-D-glucopyrancoside, leucopelargonidin-3-O-β-D-glucopyranoside, leucopelargonidin-3-O-α-L-rhamnopyranoside	All of which are known to reduce hyperglycemia (Ahmed and Urooj, 2009)
5	Lupeol	Showed elevated serum insulin level and concomitant reduction of serum glucose (Gupta *et al.,* 2012); Has potential anti-diabetic activity (Alam *et al.,* 2012)
6	Polyphenolic compounds	Have anti-oxidant and free radical scavenging properties that might be responsible for the anti-diabetic activity (Heroor *et al.,* 2013)
7	Saponins	Well known for their anti-diabetic activities by different mechanisms (Varma *et al.,* 2009)
8	Tannins	Known to possess anti-diabetic activity (Vivek *et al.,* 2010); Have potential hypoglycemic effect (Rizvi and Mishra, 2013)

Table 03. Experimental methods followed by various scientists for *Ficus racemosa*

Plant parts used	Animal model used	Extract type	Dose	Dura-tion	Route	Reference
Root	*In vivo*. Adult albino Wistar rat of either sex weighing between 150-240 g	Methanolic	100,200 and 400mg/kgbw	15 days	Oral	Varma *et al.,* 2009
Root & Bark	*In vivo*. Male Wistar albino rats having a weight of 170-220 g	Ethanolic	200 and 400mg/kgbw	4 weeks	Oral	Samyal *et al.,* 2014
Bark	*In vivo*. Swiss albino mice and rat of either sex, weighing 25-30 g and 150-200 g, respectively	Methanolic	100 and 200 mg/kgbw	21 days	Oral	Heroor *et al.,* 2013
Bark	*In vivo*. Sprague-Dawley rat of either sex; weighing 200-220g	Aqueous & Alcoholic	400mg/kgbw	21 days	Oral	Sachan *et al.,* 2009
Bark	*In vivo*. Albino Wistar male rat 7 to 8 weeks old; weighing 150-200g	Ethanolic	300mg/kgbw	45 days	Oral	Sophia and Manoharan, 2007
Stem bark	*In vivo*. Healthy adult male Wistar rat between 8-9 weeks of age; weighing 140-160g	Bark powder & Aqueous extract	500mg/kgbw	6 weeks	Oral	Ahmed and Urooj, 2009
Leaf	*In vivo*. Male and female Wistar albino rat having weight 180-230g	Methanolic (50% & 70%)	250 and 500mg/kgbw	4 weeks	Oral	Maurya *et al.,* 2011
Leaf	*In vivo*. Albino Wistar rat of either sex; 200-250g	Ethanolic	100, 200 and 300mg/kgbw	Single dose	Oral	Patil *et al.,* 2010
Leaf	*In vivo*. Male albino rat; 180-210g	Ethanolic	100, 250 & 500mg/kgbw	10 days	Oral	Vivek *et al.,* 2010
Fruit	*In vivo*. Sprague-Dauley rat of either sex, weighing 200-250g	Ethanolic	200mg/kgbw	21 days	Oral	Ramana *et al.,* 2011
Fruit	*In vivo*. Swiss albino mice aged 4-5 weeks, average weight 20-25g	Ethanolic	100 and 200mg/kgbw	14 days	Oral	Zulfiker *et al.,* 2011

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Phyto-chemicals and their anti-diabetic roles

All parts of the *Ficus racemosa* plants possess diverse phyto-chemicals which are enlisted in table 01. Among them, some phyto-chemicals have potent anti-diabetic principle which is given in table 02.

Summary of experimental procedures

Scientists used a number of experimental methods to show the anti-diabetic potentials of *Ficus racemosa*. These methods are summarized in table 03.

III. Results and Discussion

Physiological (body weight) effects of the extracts

Increased breakdown of glycogen and pronounced gluconeogenesis in diabetes might be responsible for the reduction in body weight of diabetic animals (Sophia and Manoharan, 2007). Table 04 shows an increase in the body weight in *Ficus racemosa* plants extracts treated diabetic animals with respect to diabetic control may be due to the protective effect of the extract in controlling muscle wasting, *i.e.*, reversal of gluconeogenesis and may also be due to the improvement in insulin secretion and glycemic control. According to the literature, *F. racemosa* bark methanolic extract @ 200mg/kgbw showed the best improvement in body weight of experimental animals.

Hypoglycemic effects

Excessive hepatic glycogenolysis and gluconeogenesis associated with decreased utilization of glucose by tissues is the fundamental mechanism underlying hyperglycemia in the diabetic state (Latner, 1958). Researchers used a number of doses in order to scientifically validate the therapeutic preparation of *Ficus racemosa* plants in the control of diabetes. Hypoglycemic changes reported by various scientists on application of *Ficus racemosa* are enlisted in table 05. *F. racemosa* bark aqueous extract @ 500mg/kgbw (66%) and ethanolic extract @ 300mg/kgbw (65.7%) showed the best hypoglycemic results.

Table 04. Body weight changes reported by various scientists on application of *Ficus racemosa*

Increase	Decrease	Reference
In compared to the diabetic control 100 mg/kgbw: 4.67%, 200 mg/kgbw: 4.96%, 400 mg/kgbw: 6.88%	-	Varma *et al.,* 2009
-	100 mg/kgbw: 26.21%, 250 mg/kgbw: 11.19%, 500 mg/kgbw: 09.44%	Vivek *et al.,* 2010
100 mg/kgbw: 5.63%, 200 mg/kgbw: 7.83%	-	Heroor *et al.,,* 2013
In compared to the diabetic control 300 mg/kgbw: 16.65%	-	Sophia and Manoharan, 2007
Bark: 200 mg/kgbw-14.17%, 400 mg/kgbw-23.30%	-	Samyal *et al.,* 2014

Table 05. Hypoglycemic changes reported by various scientists on application of *Ficus racemosa*

Decrease	Reference
100 mg/kgbw: 33.85%, 200 mg/kgbw: 41.91%	Zulfiker *et al.,* 2011
100 mg/kgbw: 51.23%, 200 mg/kgbw: 64.55%	Heroor *et al.,* 2013
In compared to the diabetic control 300 mg/kgbw: 65.70%	Sophia and Manoharan, 2007
Aqueous extract: 27.01%,	Sachan *et al.,* 2009

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Ethanolic extract: 45.03% 100 mg/kgbw: 12.46%, 250 mg/kgbw: 11.40%, 500 mg/kgbw: 33.97%	Vivek *et al.,* 2010
100 mg/kgbw: 35.06%, 200 mg/kgbw: 38.03%, 300 mg/kgbw: 47.92%	Patil *et al.,* 2010
100 mg/kgbw: 38.52%, 200 mg/kgbw: 49.56%, 400 mg/kgbw: 55.28%	Varma *et al.,* 2009
Bark powder: 54.00%, Bark aqueous extract: 66.00%	Ahmed and Urooj, 2009
50% methanolic extract: 250 mg/kgbw: 19.15%, 500 mg/kgbw: 09.77%; 70% methanolic extract: 250 mg/kgbw: 26.36%, 500 mg/kgbw: 09.65%	Maurya *et al.,* 2011
Bark: 200 mg/kgbw: 39.66%, 400 mg/kgbw: 42.24%; Root: 200 mg/kgbw: 38.85%, 400 mg/kgbw: 41.20%	Samyal *et al.,* 2014

Current state, limitations and remedies

Except for the use of *F. racemosa* plants for local health care needs, not much information has been available on their market potential and trading possibilities. A major factor impeding the development of the medicinal plant based industries and commercial use of these plant extract in developing countries has been the lack of information, systematic data and insufficient in-depth research on the social and economic benefits that could be derived from the industrial utilization of these medicinal plants (De Silva, 1996). As a result, the governments or entrepreneurs have not exploited the real potential of these plants. In developing countries, diabetes-specific barriers include lack of patient education about diabetes and diabetes management, stigmatization, too little/weak diagnosis and treatment facilities, negligence, poor training of healthcare professionals (HCPs) and the cost of the anti-diabetic products. Changing diabetes situation in Bangladesh requires partnerships with public and private sectors to strengthen the healthcare system, patient empowerment, access to treatment and advocacy combined with patient-focused investments in the quality of healthcare delivery. Several authors are currently being undertaken to isolate the active compounds by bioassay-guided fractionation from the species that showed high biological activity during screening (Pathak and Das, 2013). Studies on such plants with respect to their efficacy, safety profile, adverse interaction, proper standardization, etc. need to be conducted with utmost priority not only by the respective manufacturers but also by the pharmacy, pharmacognosy and medicinal enterprises.

Future prospect

Majority of experiments confirmed benefits of *F. racemosa* in the management of diabetes mellitus. Numerous mechanisms have been proposed for this plant extracts. All of these actions may be responsible for the reduction of diabetic complications (Bnouham *et al.,* 2006). There occurs a selective decrease in the hyperglycemic state after the administration of extracts of different parts of the plant, which may be mediated through a number of bioactive compounds present in the extract (Khan *et al.,* 2011). Herbal drugs have increased in popularity due to their natural origin, lesser side effects and low cost. It is recommended that the plant extract of *F. racemosa* can be successfully utilized in combination for the cure of diabetes and related diseases due to their hypoglycemic action. Polyherbal therapy is said to be a better choice in the treatment of diabetes mellitus having the advantage of producing maximum therapeutic efficacy with minimal side effects. This may provide synergistic, potentiative, agonistic/antagonistic pharmacological properties within themselves because of the presence of vast range of phytobioactive constituents (Raghavendra *et al.,* 2011). This also gives an opportunity to reduce the dose of herbs used for glycemic control in order to avoid the burden of herbal overdosing. Therefore, such combined therapy might be the key future driving force in the realm of green pharmacology and pharmacognosy (Rawat *et al.,* 2012).

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IV. Conclusion

The plant parts of *F. racemosa*, which has been used as a crude drug for the welfare of mankind in old civilization, is now of a matter of concern due to its unexplored potentials obtained by various modern techniques. *F. racemosa* possess compounds that have potential anti-diabetic activities as discussed in the present paper. Such knowledge can be applied in future studies aimed at a safe, evidence-based use of traditional medicinal plants in global phyto-pharmacotherapy and also for the discovery of novel leads for herbal drug development, might be useful for the developing as well as the developed countries.

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