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**Research Article**

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# *In vivo* Anti-Hyperglycemic Activity of *Ficus amplissima Smith* Bark Extracts

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**ABSTRACT**

*In the present investigation, in vivo antihyperglycemic activity of bark extracts of Ficus amplissima Smith. have been reported. Treatment of diabetic rats with bark extracts caused significant reduction in fasting blood glucose level in a dose dependent manner and after 14th days of treatment with extracts the body weight was significantly increased compared to the initial day. The result of present investigation reveals that the bark of the F. amplissima plant has potential biological activity, therefore suggested for further studies for purification and isolation of active phytoconstituents.*

**Keywords**: *F. amplissima*; Anti-hyperglycemic; Nicotinamide; Streptozotocin

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## INTRODUCTION

Diabetes mellitus is an endocrine metabolic disorder characterized by disarrangements in carbohydrates, proteins and fat metabolism arising as a consequence of a relative or absolute deficiency of insulin secretion and resistance to insulin action or both [1]. World Health Organization estimated the diabetic population is likely to increase up to 300 million by the year 2025 and this is a major and fast growing public health problem throughout the world [2]. Sulfonylureas, biguanides and glinides are currently available therapies for diabetes. Many of them have a number of serious adverse effects. Therefore, nowadays the search for supplementary effective and safer antihyperglycemic agents is one of the important areas of investigation.

Over the years, various medicinal plants and their extracts have been reported to be effective in the treatment of diabetes [3]. On basis of this, plants have rich sources of antidiabetic and antioxidant agents such as flavonoids [4], alkaloids, terpenoids [5] and other related polyphenols [6]. The plant *F. amplissima Smith* belongs to the family Moraceae, it is a popular folk medicine and has been studied for jaundice. The leaves have potential anti-inflammatory, wound healing and antioxidant properties [7]. The acetone extract of the bark possesses antioxidant, anti-inflammatory activity and about 27 phytoconstituents analyzed by GC-MS [8] and the bark has potential antidiabetic activity in streptozotocin-induced diabetic rats [9].

In our previous study we describe the qualitative and quantitative phytochemical analysis of bark of *F.amplissima*indicated that, the bark of plant is rich in phytoconstituents like flavonoids, saponins, glycosides, alkaloids and phenolic compounds [10]. In view of the above facts, in the present investigation we have carried out the antihyperglycemic activity of *F. amplissima Smith* bark extracts.

## EXPERIMENTAL SECTION

### Material and methods

**Kits and chemicals:**

Streptozotocin (STZ) was purchased from Sigma-Aldrich. Nicotinamide was purchased from Ranbaxy Chemicals Ltd., Mumbai, India. Glucometer and Glucometer strips for measurement of fasting blood glucose were purchased from a local vendor, manufactured by Accu-check Advantage, Roche diagnostics Mannheim, Germany. Glibenclamide and other chemicals were obtained from local firms and were of analytical grade.

**Collection and identification of plant:**

Healthy stem bark of *F. amlissima* was collected from Bhadra Reserve Forest, Shivamogga, Karnataka, India. Plant was identified as *F. amlissima*with the help of faculty of Department of Applied Botany, Kuvempu University, Shankaraghatta, Karnataka, India. Bark was separated from unwanted materials, brushed, shade dried and powdered mechanically.

**Preparation of plant extract:**

500 g of stem bark powder was defatted using petroleum ether and sequentially extracted with methanol and double distilled water in soxhlet apparatus and extracts were referred as *F. amlissima* methanol extract (FAME) and *F. amlissima* aqueous extract (FAAE) respectively. The extracts were filtered and concentrated in vacuum using rotary flash evaporator (BuchiRotavapor R-200) and the obtained crude extracts were stored in desiccator until further studies.

**Anti-hyperglycemic activity**

**Oral glucose tolerance test in normal rats:**

Overnight fasted normal rats were divided into eight groups of six rats each. They were orally administered with vehicle, FAME and FAAE (250, 500 and 1000 mg/kg) and glibenclamide (60 mg/kg), respectively. Glucose (2 g/kg) was fed 30 min after the administration of extract [11]. Blood was withdrawn through the tail vein at 0, 30, 60 and 120 min of glucose administration.

**Induction of non-insulin-dependent diabetes mellitus (NIDDM):**

Diabetes mellitus was induced in overnight fasted adult Wistar strain albino male rats by a single intraperitoneal injection of freshly prepared STZ (60mg/kg b. wt) in 0.1 M citrate buffer (pH 4.5) in a volume of 1 ml/kg body weight. After15 min the intraperitoneal injection administration of 120 mg/kg of nicotinamide was dissolved in normal saline [12]. Diabetes was confirmed by the elevated glucose levels in plasma, determined at 72 hr. Rats with a fasting plasma glucose range of 280-350 mg/dL were considered diabetic and used for the study.

Animals were divided into nine groups of six rats each.
Group I: normal control rats administered gum acacia (2%) daily for 14 days;
Group II: diabetic control rats administered gum acacia (2%) daily for 14 days;
Group III: diabetic rats administered FAME (250 mg/kg); Group IV: diabetic rats administered FAME (500 mg/kg);
Group V: diabetic rats administered FAME (1000 mg/kg); Group VI: diabetic rats administered FAAE (250 mg/kg);
Group VII: diabetic rats administered FAAE (500 mg/kg);
Group VIII: diabetic rats administered FAAE (1000 mg/kg);
Group IX: diabetic rats administered glibenclamide (0.25 mg/kg). The extract and drug was administered for 14 days.

The effect of administration of extracts to normal and diabetic rats was determined by measuring fasting plasma glucose levels by enzymatic glucose oxidase method using a commercial glucometer. Fasting plasma glucose was estimated on days 0, 1, 3, 5, 7, and 14 of extract administration. The change in the body weight at initial and final was noted.

## RESULT AND DISCUSSION

The qualitative phytochemical analysis of bark extracts of *F. amplissima* indicated that, the bark of plant is rich in phytoconstituents like flavonoids, saponins, glycosides, alkaloids and phenolic compounds. The presence of these phytoconstituents in plants may in part be responsible for the observed significant activity either single or in synergy with one another.

**Anti-hyperglycemic activity**

**Oral glucose tolerance test in normal rats:**

Table 1 shows the oral glucose tolerance levels of *F. amplissima* bark extracts. After glucose load, the administration of 250, 500 and 1000 mg/kg of extracts decreased the elevation of serum glucose level significantly ($P \leq 0.005$) at 120 min.

**Table 1: Effect of *F. amplissima* bark extracts on oral glucose tolerance**

| Group | Blood glucose levels (mg/dl) | | | |
|---|---|---|---|---|
| | 0min | 30 min | 60 min | 120 min |
| Normal control | 99.87 ± 1.05 | 119.30 ± 3.02 | 116.07 ± 2.05 | 101.71 ± 1.21 |
| FAME (250 mg/kg) | 94.56 ± 1.68 | 118.52 ± 2.11 | 117.12 ± 2.29 | 115.91 ± 2.08 |
| FAME (500 mg/kg) | 95.08 ± 2.44 | 117.02 ± 1.01 | 116.80 ± 1.91 | 104.04 ± 1.90 |
| FAME (1000 mg/kg) | 97.42 ± 3.11 | 122.03 ± 2.21 | 112.56 ± 2.056 | 98.56 ± 3.00 |
| FAAE (250 mg/kg) | 99.84 ± 2.15 | 117.64 ± 2.23 | 112.54 ± 1.55 | 111.64 ± 2.01 |
| FAAE (500 mg/kg) | 96.08 ± 2.99 | 116.05 ± 2.05 | 114.04 ± 1.05 | 111.70 ± 1.25 |
| FAAE (1000 mg/kg) | 98.98 ± 1.08 | 115.45 ± 1.75 | 105.35 ± 2.40 | 99.02 ± 3.08 |
| Glibenclamide (60mg/kg) | 96.62 ±2.44 | 115.34 ± 2.66 | 99.03 ± 1.26 | 89.09 ± 2.06 |

Values indicate mean ± SEM (n = 6).

**Effect of extracts on fasting blood glucose and body weight in STZ-Nicotinamide induced diabetic rats**

The antidiabetic activity results revealed that, decreased in blood glucose level in STZ-Nicotinamide induced diabetic rats treated with bark extracts showed the antidiabetic potentiality of the plant. Extracts administered at three different doses of 250mg/kg, 500mg/kg, 1000mg/kg to STZ- Nicotinamide treated diabetic rats caused significant ($P<0.001$) reduction of blood glucose levels which was related to dose and duration of treatment (Table 2). Among the tested bark extracts, FAME showed promising activity at 500mg/kg, 1000mg/kg, while FAAE showed moderate activity. The order of antidiabetic activity of extracts FAME > FAAE. After $14^{th}$ days of treatment with extracts the body weight was significantly increased compared to the initial day. All the three doses showed significant improvement in body weight compared to diabetic control (Table 3).

**Table 2: Effect of extract of *F. amlissima* bark on fasting blood glucose levels (mg/dl) of normal and diabetic rats**

| Group (n=6) | Treatment | Fasting plasma glucose concentration ( mg/dl) | | | | | |
|---|---|---|---|---|---|---|---|
| | | 0th day | 1st day | 03ed day | 5th day | 7th day | 14th day |
| I | Normal control | 83.50±2.11 | 101.45 ±2.10 | 95.03±3.07 | 82.42 ± 3.78 | 98.16±4.21 | 90.01±4.77 |
| II | Diabetic control | 345.64±1.22$^{ac}$ | 360.94 ±10.27$^{ac}$ | 404.78±3.88$^{ac}$ | 390.18 ±13.08$^{ac}$ | 373.05 ±15.24$^{ac}$ | 382.43±8.90$^{ac}$ |
| III | Diabetic + FAME (250mg/kg) | 224.45±8.47 | 215.83±9.62 | 243.50±7.17 | 253.83±13.09 | 236.5±87.02 | 327.16±16.35 |
| IV | Diabetic + FAME (500mg/kg) | 250.33±15.87 | 253.83±14.99 | 299.16±21.49 | 242.45±8.24 | 226.16±14.57 | 234.83±23.47 |
| V | Diabetic + FAME (1000mg/kg) | 258.5±15.73 | 257.66±19.68 | 233.67±17.03 | 233.67±17.03$^{a}$ | 240.83±24.05 | 223.33±23.73$^{abc}$ |
| VI | Diabetic + FAAE (250mg/kg) | 252.01±16.12 | 220.16±13.01 | 266.67±4.41 | 248.5±15.49 | 279.16±19.4 | 287.83±38.65$^{ac}$ |
| VII | Diabetic + FAAE (500mg/kg) | 259.33±21.55 | 241.66±17.84$^{ab}$ | 221.33±26.92 | 260.83±13.30 | 279.83±18.94$^{a}$ | 262.50±23.23$^{ac}$ |
| VIII | Diabetic + FAAE (1000mg/kg) | 246.66±11.51$^{a}$ | 236.66±15.46 | 262.83±19.40 | 262.83±19.40$^{a}$ | 258.00±13.93$^{a}$ | 242.84±14.84$^{abc}$ |
| XI | Diabetic + glibenclamide (0.25 mg/kg) | 251.72±8.07$^{ab}$ | 201.02±14.11 | 187.38±9.09 | 173.45±5.62 | 99.03±7.86$^{ab}$ | 102.87±6.20$^{ab}$ |

Values are mean± SEM of 6 animals in each group. a: P<0.05 comparing with the normal; b:P<0.05 comparing with diabetic control: c: P<0.05 comparing with glibenclamide treated group.

The *in vivo* results obtained in STZ–Nicotinamide induced type 2 diabetic rats model indicated that the crude extract of *F. amplissima* bark at a concentration of 1000 mg/kg body weight, has the ability to lower blood glucose levels. The extracts exhibited a significant dose dependent antihypoglycemic activity and these results are comparable with standard glibenclamide. In general there is very little biological knowledge on the specific mode of action in the treatment of diabetes, probably secondary metabolites like alkaloid, flavonoid, polyphenolics and saponinsins suppressed the glucose level and increased their hepatic glucokinase activity by enhancing the insulin release from

pancreatic islets i.e., its action to release bound insulin from regenerated β cells by inhibiting ATP sensitive $K^+$ channels like glibenclamide or may be pancreatic secretion of insulin from regenerated β-cells. In STZ–Nicotinamide induced type 2 diabetic rat models, the body weight is reduced due to destruction of muscle tissue and loss of protein contents. The improvement of body weight in rats treated with extract signifies its reversal of gluconeogenesis, in turn reflect its ability to reduce hyperglycemia.

**Table 3: Effect of extracts of *F. apmlissima* bark on body weight in STZ-Nicotinamide induced diabetic rats**

| Group (n=6) | Treatment | Body weight | |
|---|---|---|---|
| | | 0th day | 14th day |
| I | Normal control | 195.01 ± 4.08 | 224.09 ± 9.94 |
| II | Diabetic control | 190.56 ± 9.45 | 168.13 ± 15.83 |
| III | Diabetic + FAME (250mg/kg) | 201.01 ± 8.45 | 213.68 ± 7.38 |
| IV | Diabetic + FAME (500mg/kg) | 195.85 ± 4.08 | 228.07 ± 15.07 |
| V | Diabetic + FAME (1000mg/kg) | 200.98 ± 4.11 | 231.57 ± 8.76 |
| VI | Diabetic + FAAE (250mg/kg) | 196.78 ± 7.05 | 219.45 ± 10.08 |
| VII | Diabetic + FAAE (500mg/kg) | 189.86 ± 5.75 | 229.86 ± 5.75 |
| VIII | Diabetic + FAAE (1000mg/kg) | 200.07 ± 11.75[a] | 240.08 ± 9.81[a] |
| XI | Diabetic + glibenclamide (0.25 mg/kg) | 197.00 ±9.03[a] | 218.07 ± 10.57[a] |

Values are mean± SEM of 6 animals in each group. a: P<0.05 comparing with the normal; b:P<0.05 comparing with diabetic control: c: P<0.05 comparing with glibenclamide treated group.

The antihypoglycemic activity of *F. amplissima* bark are due to the presence of phytoconstituents, γ-sitosterol, olean-12-en-3-one, lupeol, 2-hydroxy-1-(hydroxymethyl)ethyl ester, menthol and stearaldehyde. Several studies on these compounds have demonstrated antidiabetic, antioxidant, antimicrobial, anticancer and anti-inflammatory properties [13-16]. Polyphenols and flavonoids in the bark extract are well known for their antioxidant properties, they may scavenge the free radicals generated during diabetes [17, 18] and these might have crucial roles in the observed hypoglycemic activity of the bark.

## CONCLUSIONS

In conclusion, it could be cogitated that the observed biological activity of *F. amplissima* bark might be related to the presence of flavonoids and polyphenolic as active phytoconstituents. It is recommended that more research work to be conducted to found out the presence of bioactive compounds in the plant and formulated into appropriate doses for the treatment of infectious disease.

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