

## FICUS EXASPERATA: EFFECTS ON DIABETES MELLITUS IN AN EXPERIMENTAL RAT MODEL

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### ABSTRACT

Effect of *Ficus exasperata* (Vahl) leaf on hyperlipidaemia, hypercholesterolaemia and hyperketonaemia associated with alloxan-induced diabetes mellitus were studied. One week oral administration of an aqueous extract of the leaf to alloxan-induced diabetic rats decreased plasma total triacylglycerol levels. Similarly, cholesterol and  $\beta$ -hydroxybutyrate concentrations were significantly ( $p < 0.05$ ) reduced. Results indicate that *F. exasperata* leaf possesses effective lipid lowering properties in diabetic rats.

**KEYWORDS:** *Ficus exasperata*, alloxan-induced diabetes mellitus, triacylglycerol, cholesterol,  $\beta$ -hydroxybutyrate.

### INTRODUCTION

The possible medicinal use of the vegetation as cheaper or alternative therapies is gaining widespread interest throughout the world. Several plants are being investigated for their hypoglycaemic and hypolipidaemic properties. Among these are *Tinospora cordifolia*, *Aloe vera*, *Caesalpinia bonducella* and *Sambucus nigra* (Wadood *et al*, 1992; Yongchaiyadhas *et al*, 1996; Sharma *et al*, 1997; Gray *et al*, 2000).

*Ficus exasperata* Vahl (family: Moraceae) commonly known as "sandpaper" leaf was reported to have a number of useful medicinal attributes including ophthalmic, antihelmintic, haemostatic and anticoagulant properties (Chhabra *et al*, 1984; Kone-Bamba *et al*, 1987). Oral administration of the aqueous extract to alloxan-induced diabetic rats was shown to reduce significantly, blood and urine glucose levels (Nimenibo-Uadia and Osagie, 2001). However, the risk of vascular complications in diabetes mellitus will be reduced by control not only of blood glucose levels, but also lipid levels, blood pressure and weight (Williams, 1994).

The present study was undertaken to further evaluate the possible presence of antidiabetic activities in *F. exasperata* leaf by investigating its effects on triacylglycerol, cholesterol and  $\beta$ -hydroxybutyrate in alloxan-induced diabetic rats.

### MATERIALS AND METHODS

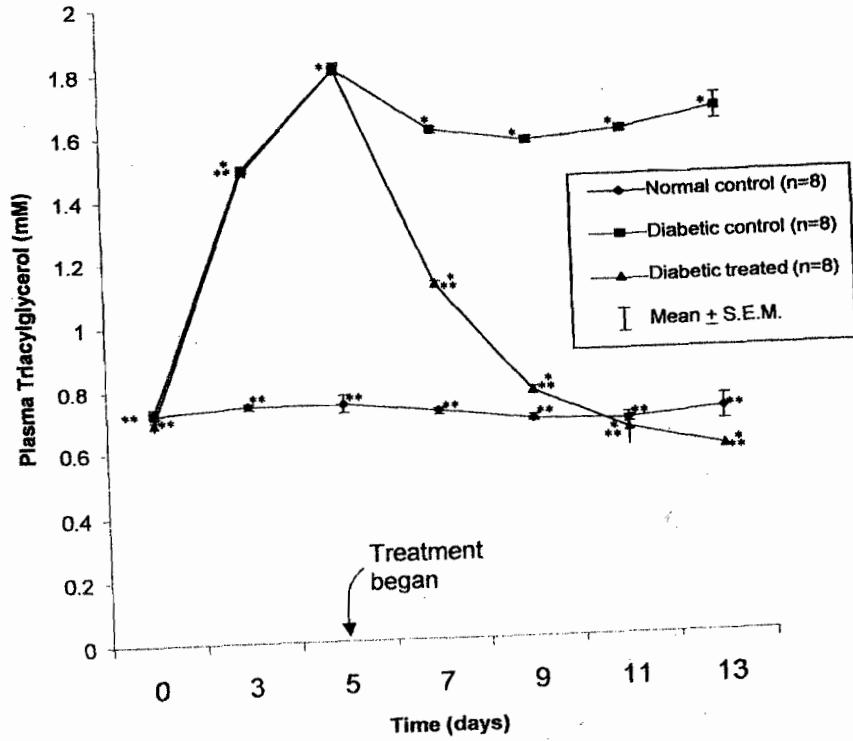
**Animals.** Twenty-four albino rats (Wistar strain) weighing between 180-250g in three groups of 8

rats were utilized. All rats were given distilled water and standard pellet diet (Pfizer Feeds Plc., Nigeria) *ad libitum*.

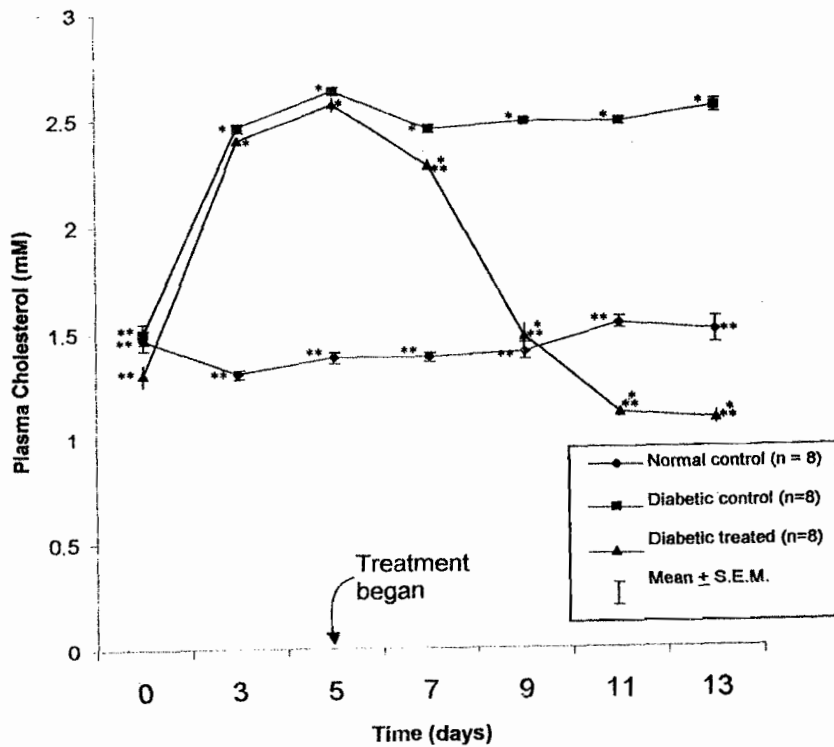
**Plant Material.** Fifty grams of the dried and pulverized leaves of *F. exasperata* obtained in and around the University of Benin grounds were boiled in 1 litre of distilled water. After 10 mins, the suspension was filtered and the filtrate evaporated to dryness. When needed, a 5% portion of the resulting material stored at  $-4^{\circ}\text{C}$ , was reconstituted in distilled water. This solution was used as stock crude drug.

**Experimental Procedure.** Induction of diabetes in rats was done within 72h by the intraperitoneal administration of alloxan monohydrate (Sigma, St. Louis, MO, USA) dissolved in distilled water (5%) in a dose of 100mg/kg body weight. Rats were rested for 3 days to allow glucose levels stabilize. Diabetes was confirmed in induced rats by testing for glucosuria using glucose indicator sticks (Bayer Diagnostics, Basingstoke, UK) and for hyperglycaemia by testing fasting blood glucose levels. Only rats with fasting blood glucose  $>10\text{mM}$  were considered diabetic and used for further experimentation (Al-Awadi *et al*, 1991). The diabetic animals were then divided into diabetic control (Group 1) and test rats (Group 2). Untreated rats (Group 3) served as normal control and were injected with an equivalent volume of the vehicle.

Treatment of test rats began on Day 5 (post-alloxan). The crude aqueous extract of the leaf, at a dosage of 400mg/kg body weight (arrived at after a preliminary study) was utilized. The extract was administered orally by



**Figure 1:** Plasma triacylglycerol response of diabetic rats during oral administration of *F. exasperata* aqueous leaf extract.  
 \*As compared with normal rats within each group, (Day 0),  $p < 0.05$   
 \*\*As compared with diabetic rats pre-treatment, (Day 5),  $p < 0.05$



**Figure 2:** Plasma cholesterol response of diabetic rats during oral administration of *F. exasperata* aqueous leaf extract.  
 \*As compared with normal rats within each group, (Day 0),  $p < 0.05$   
 \*\*As compared with diabetic rats pre-treatment, (Day 5),  $p < 0.05$

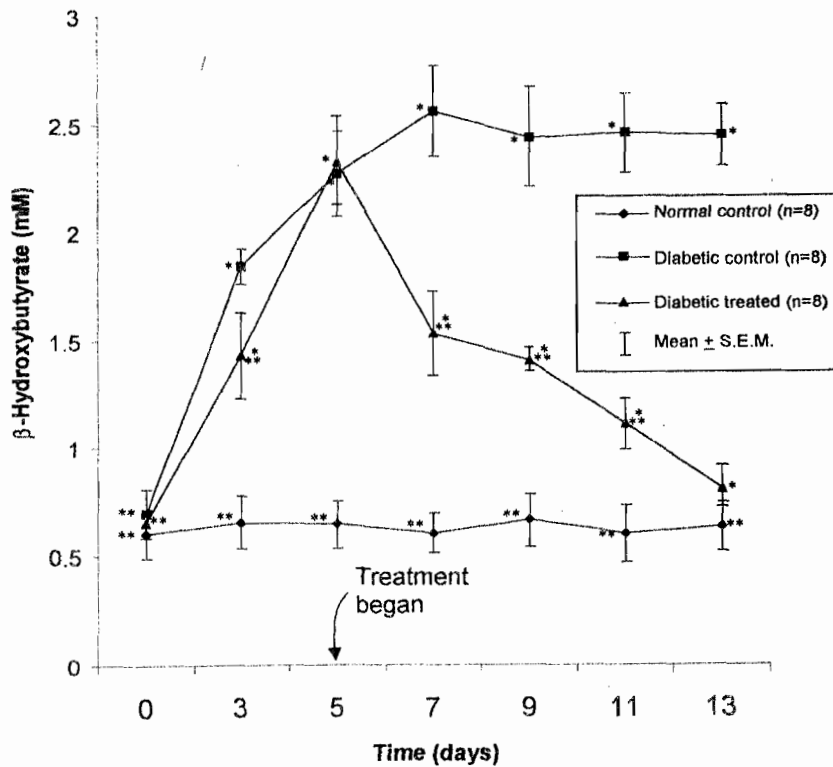


Figure 3: Plasma  $\beta$ -hydroxybutyrate response of diabetic rats during oral administration of *F. exasperata* aqueous leaf extract.

\*As compared with normal rats within each group, (Day 0),  $p < 0.05$

\*\*As compared with diabetic rats pre-treatment, (Day 5),  $p < 0.05$

means of a gavage to the test rats (Group 2) once a day, for seven consecutive days. Fasting blood samples for analyses were collected into ice-cold sodium fluoride treated tubes and centrifuged (MSE minor bench centrifuge). Plasma glucose levels were assayed spectrophotometrically (Pye Unicam SP 1800 Ultraviolet Spectrophotometer) using a Sigma Diagnostic glucose oxidase kit (Procedure No. 510). Total triacylglycerol, cholesterol and  $\beta$ -hydroxybutyrate concentrations were also determined using Sigma Diagnostic kits (Procedures No. 337, 352 and 310-UV respectively).

**Statistical Analysis.** Data were expressed as mean  $\pm$  SEM. Differences between groups were evaluated using Student's t-test (Woodson, 1987). Statistical significance was set at  $p < 0.05$ .

## RESULTS AND DISCUSSION

Diabetes mellitus in induced rats was confirmed by fasting blood glucose levels in excess of 10mM (Al-Awadi *et al*, 1991).

Alloxan-induced diabetic rats demonstrated a spectrum of severity with hypertriacylglycerolaemia ( $1.48 \pm 0.01 - 1.80 \pm$

$0.02\text{mM}$ ), hypercholesterolaemia ( $2.40 \pm 0.01 - 2.63 \pm 0.02\text{mM}$ ) and hyperketonaemia ( $1.43 \pm 0.2 - 2.56 \pm 0.21\text{mM}$ ). Hyperglycaemic values ranged from  $7.01 \pm 0.28$  to  $13.53 \pm 0.29$  mM (laboratory note). Insulin is produced by  $\beta$ -cells of the islets of Langerhans and in alloxan-induced diabetes, the  $\beta$ -cells are destroyed (Chakravarthy *et al*, 1982). Hyperglycaemia occurs because of decreased entry of glucose into cells, decreased utilization of glucose by various tissues and increased production of glucose (gluconeogenesis) by the liver (Granner, 1996). In severe insulin deficiency, there is accelerated lipolysis, which results in elevated plasma triacylglycerol levels

(hyperlipidaemia) and acetyl-CoA (Granner, 1996). The accumulation of acetyl-CoA leads to hypercholesterolaemia since, acetyl-CoA is a key substrate in the biosynthesis of cholesterol (Granner, 1996). Ketosis occurs in the absence of insulin because there is increased fat breakdown to acetyl-CoA (Rang *et al*, 1995). Little of the acetyl-CoA is metabolized by the citric acid cycle, while the remainder is converted to aceto-acetate,  $\beta$ -hydroxybutyrate and acetone in the absence of carbohydrate metabolism (Rang *et al*, 1995; Granner, 1996) These observations are consistent with the

results of this study (Figures 1, 2 and 3).

Administration of distilled water to control animals (normal and diabetic) did not produce any significant change ( $p > 0.05$ ) on the plasma total triacylglycerol, cholesterol and  $\beta$ -hydroxybutyrate concentrations (Figures 1, 2 and 3). However, when aqueous *F. exasperata* extract was administered to the alloxan-induced diabetic rats, the hitherto elevated plasma levels of triacylglycerol, cholesterol and  $\beta$ -hydroxybutyrate were significantly ( $p < 0.05$ ) reduced. Fasting triacylglycerol concentrations fell to  $0.58 \pm 0.05$  from  $1.80 \pm 0.01$  mM. Cholesterol levels were decreased to  $1.08 \pm 0.03$  from  $2.57 \pm 0.03$  mM while  $\beta$ -hydroxybutyrate concentrations fell to  $0.80 \pm 0.11$  from  $2.33 \pm 0.21$  mM after seven days (Figures 1, 2 and 3).

In conclusion, this study has shown that the aqueous extract of *F. exasperata* leaf when administered orally is able to counter some negative effects of diabetes mellitus, such as hyperlipidaemia, hypercholesterolaemia and hyperketonaemia.

#### ACKNOWLEDGEMENT

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#### REFERENCES

- Al-Awadi, F., Fatania, H. and Shamte, U. 1991. The effect of a plant mixture extract on liver gluconeogenesis in streptozotocin-induced diabetic rats. *Diabetes Research* 18: 163-168.
- Chakravarthy, B.K., Gupta, S and Gode, K.D. 1982. Functional beta cell regeneration in the islets of pancreas in alloxan-induced diabetic rats by (-)-epicatechin. *Life Sciences* 31: 2693-2697.
- Chhabra, S.C., Uiso, F.C. and Mshiu, F.N. 1984. Phytochemical Screening of Tanzanian Medicinal Plants. *J. Ethnopharmacol* 11(2): 157-179.
- Granner, D.K. 1996. Hormones of the Pancreas and Gastrointestinal Tract. In: R.K. Murray, D.K. Granner, P.A. Mayes and V.W. Rodwell (Editors) *Harper's Biochemistry* (24<sup>th</sup> ed.). Appleton and Lange, Connecticut, pp. 586-587.
- Gray, A.M., Abdel-Wahab, Y.H.A. and Flatt, P.R. 2000. The traditional plant treatment, *Sambucus nigra* (elder), exhibits insulin-like and insulin-releasing actions *in vitro*. *J. Nutr.* 130: 15-20.
- Sharma, S.R., Dwivedi, S.K. and Swarup, D. 1997. Hypoglycaemic, antihyperglycaemic and hypolipidemic activities of *Caesalpinia bonducella* seeds in rats. *J. Ethnopharmacol.* 58(1): 39-44.
- Sigma Diagnostics: Quantitative, Enzymatic (Glucose Oxidase) Determination in Whole Blood, Serum or Plasma at 425-475nm (Procedure No. 510, 1990).
- Sigma Diagnostics: Quantitative, Enzymatic Determination of Glycerol, True Triglycerides, and Total Triglycerides in Serum or Plasma at 540nm (Procedure No. 337, 1990).
- Sigma Diagnostics: Quantitative, Enzymatic Determination of Total Cholesterol in Serum or Plasma at 500nm (Procedure No. 352, 1991).
- Sigma Diagnostics: Quantitative, Enzymatic Determination of  $\beta$ -Hydroxybutyrate in Serum or Plasma at 340nm (Procedure No. 310-UV, 1987).
- Kone-Bamba, D., Pelissier, Y., Ozoukou, Z.F. and Kouao, D. 1987. Haemostatic activity of 216 plants used in traditional medicine in Ivory Coast. *Planta Med. Phytother.* 21(2): 122-130.
- Nimenibo-Uadia, R. and Osagie, A.U. 2001. Effect of *Ficus exasperata* (Vahl) Aqueous Leaf Extract on Normal and Alloxan-Diabetic Rats. *Nig. J. Biochem. Mol. Biol.* 16(1): 67-71.
- Rang, A.P., Dale M.M. and Ritter, J.M. 1995. *Pharmacology* (3<sup>rd</sup> ed.). Churchill Livingstone, New York, pp. 410-416.
- Wadood, N, Wadood, A. and Shah, S.A.W. 1992. Effect of *Tinospora cordifolia* on Blood Glucose and Total Lipid Levels of Normal and Alloxan-Diabetic Rabbits. *Planta Med.* 58: 131-136.
- Williams, G. 1994. Management of non-insulin dependent diabetes mellitus. *Lancet* 343: 95-100.
- Woodson, R.F. 1987. *Statistical Methods for the Analysis of Biochemical Data. Probability and Mathematical Statistics*, Wiley, Chichester, pp. 315-316.
- Yongchaiyadhas, S., Rungpitarangsi, V., Bunyapraphatasara, N and Chokechajaroenpom, O. 1996. Anti-diabetic Activity of *Aloe vera* juice: Clinical trials in new cases of diabetes mellitus. *Phytomedicine* 3: 241-243.