

## Efficacy and safety of *Englerina lecardii* (Engl.) Balle in the treatment of type 2 diabetes

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### To cite this article:

E. S. Balde, N. M. Balde, M. S. Traore, I. V. Camara, M. S. T. Diallo, M. A. Balde, A. Camara, A. M. Balde. Efficacy and Safety of *Englerina lecardii* (Engl.) Balle in the Treatment of Type 2 Diabetes. *Journal of Plant Sciences*. Special Issue: Ethnopharmacological Investigation of Medicinal Plants. Vol. 3, No. 1-2, 2015, pp. 24-27. doi: 10.11648/j.jps.s.2015030102.15

**Abstract:** The use of phytomedicine to treat many chronic diseases as diabetes is current in developing countries and pharmacological data in some case support this use. The aim of this study is to evaluate the efficacy and safety of *Englerina lecardii* leaves in the treatment of type 2 diabetes. An open label study design was designed to examine the effects of leave of *Englerina lecardii* at a dose of 15g/day in three divided doses during 90 days in 31 subjects with type 2 diabetes. 25 patients (9 men and 16 women ; age ) completed the study. On average, glycaemia at the end of treatment was decreased by 80 mg/dl (+xx). Only mild and temporary side effects were observed, without leading to interrupt the treatment. In conclusion, the use of *Englerina lecardii* showed significant hypoglycemic effect without any major side effect. These data need to be confirm in a standard double blinded clinical trial.

**Keywords:** *Englerina lecardii*, Loranthaceae, Type 2 Diabetes, Efficacy, Safety

## 1. Introduction

Diabetes is a metabolic disorder, which is fast growing disorder over the world. The treatment of diabetes with synthetic drugs is costly and chances of side effects are highly. Although new and more efficacious diabetes medications and improved medication delivery systems have been developed, the majority of diabetic patients do not achieve optimal blood glucose control (1), leading to poor health outcomes and needing the news alternative drugs for treatment. It is the fact that diabetes can not be cured and it has never been reported that someone had recovered totally from diabetes. (2). In developing countries herbal drugs play an important role as traditional alternative medicines (3-4), and plant drugs are frequently considered to be less toxic and free from side effects than synthetic ones (5). Use of plants may delay development of diabetic complications and can correct the metabolic abnormalities through variety of mechanisms. Moreover, during the past few years many phytoconstituents responsible for anti-diabetic effects have been isolated from

plants (6-7). The use of phytomedicine to treat many chronic diseases like diabetes is current in developing countries and pharmacological data in some case confirm this use (8-9). Ethnobotanical research has a long history of investigating plants and health conditions that are important in traditional medicine. For many years, one of the main interests of research into medicinal plants has been to identify new plant leads for drug discovery programs (10).

In Guinea many people still use traditional herbs to treat a variety of diseases including Diabetes (11-12). The use of herbal remedies is likely to be particularly important in rural area where modern medicines, when available, are too expensive. At first, an ethnobotanical survey was carried out by the Guinean “Centre de Recherche et de Valorisation des Plantes Médicinales (CRVPM)-Dubreka” in several regions to collect information on cures used in traditional treatment of diabetes. Among the collected plants in Middle Guinea *Englerina lecardii* has retained our attention.

*E. lecardii* (Loranthaceae), is a bushy parasitic plant, branches up to 60–80 cm long, on bushes and trees of the forest or savannah. It is widely distributed in Senegal, Mali, Guinea-Bissau and in Guinea. The leave of *E. lecardii*, traditionally named Sattaga bowal in Fulani, are used for treatment of diabetes mellitus in Guinea, but any clinical studies have been conducted to determine its efficacy and safety in diabetic patients. The aim of this study is to evaluate the efficacy and safety of *E. lecardii* leaves in the treatment of type 2 diabetes.

## 2. Method

### 2.1. Recruitment Protocol

An open label study design was used to examine the effects of leave of *E. lecardii* in newly diagnosed type 2 diabetes subjects who regularly attend to outpatient consultation of the diabetes clinic in the Donka University hospital Conakry. The included 31 patients were: 1) Type 2 diabetes patients with glycaemia between 175 mg/ml and 250 mg/ml, not receiving conventional treatment, 2) older  $\geq 30$  years of age and  $\leq 60$  years of age, and 3) signed consent form for participation in the study. The following exclusion criteria were applied: 1) presence of severe infectious disease, 2) retinopathy, moderate or severe renal dysfunction, severe liver dysfunction, moderate or severe heart failure, pregnancy, breastfeeding.

The protocol was approved by the Guinean Ethic Committee. Written informed consent is obtained from all the participants after a full explanation of the study. Demographic data, patient characteristics before treatment and during follow up are showed in figure 1.

### 2.2. Protocol Treatment

*E. lecardii* leaf was conditioned in a tea bag of 5 g powder which infused during 15mn. Each patient received 3 infusions per day (morning, midday and evening). Duration of treatment was 90 days for each patient.

### 2.3. Efficiency Assessments

The efficacy endpoint was the change from baseline (mean of week 12, week 6 and week 0) to the end point regarding the glycaemic level in the patients.

### 2.4. Safety Assessments

Side effects were monitored at every visit from baseline to the end of the study. Body mass index, arterial tension, Fasting complete blood count, Total cholesterol, creatinine, triglycerides, ASAT, ALAT), were also assessed at screening and end of the study.

### 2.5. Statistical Analysis

Data are expressed as mean $\pm$ SD. Values within groups were compared by paired sample Student's t-test. The tests evaluated at the 0.05 significance level.

## 3. Results

Among the 31 patients, 25 patients (9 men and 16 women) with a mean age of 49 years completed the study. 6 patients drop out (4 patients lost follow up and 2 patients retired their consentment).

### 3.1. Efficacy

The data are summarized in table I. On average for the patient, glycaemia at the end of treatment is decreased by 80 mg/dl (from 205  $\pm$  mg/dl to 125  $\pm$  mg/dl after 12 weeks of treatment;  $p < 0.001$ ).

### 3.2. Safety

10 patients (40%) reported side effects: 4 cases of diarrhea, bitterness taste after drinking the remedy in 2 cases, 1 case of polyuria, 1 case of xerostomia, and 1 case of diurnal sleepiness. The treatment produced only mild and temporary side effects, which not lead to cessation of the treatment. We observed reduction of weight, body mass index, systolic blood pressure, and diastolic blood pressure (see Table I) but these changes were not statistically significant.

**Table I.** Clinical data and glycaemia evolution during the treatment

Variables	Inclusion	Week 6	Week 12	Balance (%)*	P **
Weight (Kg)	77,28	77,32	76,81	-0,4 (-0,6%)	0,41
Body mass index (Kg/m <sup>2</sup> )	28,94	28,98	28,7	-0,2 (-0,8%)	0,53
Systolic blood pressure (mm Hg)	128,8	125,6	123,2	-5,6 (-4,4%)	0,07
Diastolic blood pressure (mm Hg)	83,9	82,8	80,8	-2,4 (-2,9%)	0,27
Glycemia (g/L)	2,1	1,5	1,3	-0,8 (-39,1%)	<0,001

**Table II.** Biological parameters evolution during the treatment

Variables	Inclusion	Week 6	Week 12	Balance (%)*	P **
ASAT (UI/L)	7,2	6,4	6,5	-0,7 (-9,5%)	0,73
ALAT (UI/L)	7,4	12,5	7,6	0,1 (+1,9%)	0,89
Total Bilirubin (mmol/L)	13,3	11,8	11,2	-2,1 (-5,8%)	0,31
Creatinin (mmol/L)	72,11	67,08	88,8	+16,7 (+23,2%)	0,38
Triglyceride (mmol/ L)	2,1	2,5	2,6	0,5 (+23,2%)	0,43
Total Cholesterol (mmol/L)	5,2	5,8	6,4	1,2 (+22,7%)	0,004

The biological parameters variations after 6 and 12 weeks of treatment are summarized in table II. We did not observe any abnormality in the complete blood count. We observed a difference at the end of treatment regarding total cholesterol (5.2 mmol/L versus 6.3 mmol/L;  $p < 0.05$ ). The other parameters (creatinine, triglycerides, ASAT, ALAT, bilirubin) did not change during treatment.

## 4. Discussion and Conclusion

The rapidly increasing incidence of diabetes mellitus is becoming a serious threat to mankind health in all parts of the world. Hence, there is a need for new antidiabetic agents which will have therapeutic efficacy as well as have less side effects. There are reports to treat diabetics with traditional medicinal plants which have fewer side effects, better effectiveness, multiple target site and are of relatively of low cost (13). In this way, a large number of plant species (*Allium sativum*, *Pterocarpus marsupium*, *Gymnema sylvestre*, *Citrullus colocynthis*, *Trigonella foenum greacum*, *Momordica charantia*, *Ficus bengalensis* etc.) with hypoglycemic properties have been described from Leguminosae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae, Araliaceae, Poaceae, Euphorbiaceae etc. (14-15).

Since a long time, *E. lecardii* is used by the Middle-Guinea's population in the management of diseases without any notified severe side effects by the traditional healers or the patient consumers. However, according to World health organization, safety considerations, regarding toxicological analysis, pre-clinical and clinical trials are essential prior to any integration of herbal medicine within the public health system (16). Upon consideration of these evidences, the therapeutic evaluation of the antidiabetic effect of the leaf of *E. lecardii* was done to measure the efficacy, tolerance and safety effects of the plant species. At a dose of 5g x 3 daily, the infusion of *E. lecardii* has shown to exert a significant anti-hyperglycaemic effect in diabetic patients after 3 months of treatment. Like the oral anti-diabetic Biguanide (17), *E. lecardii* reduced progressively the glycaemia level during the treatment. This effect was observed without any increasing body weight in these patients.

All the patients were satisfied with the medicine and did not report any major side effect preventing the continuation of their treatment. Although not significant, a slight decreasing change of systolic blood pressure (from 129 to 123 mmHg), diastolic blood pressure (from 84 to 81 mmHg), body weight (from 77.3 to 76.8 Kg), body mass index (from 28.9 to 28.7 Kg/m<sup>2</sup>) was observed. Having in mind the new American Diabetes Association (ADA, 2013) (18) recommended blood pressure goal in diabetic patients has been revised from <130/80 mmHg to <140/80 mmHg, it is important to notice the relative stability of these values during the treatment with *E. lecardii*.

An increase change of the creatinine level from the baseline (72.11 mmol/l) to the end of the treatment (week 12; 88.8

mmol/l) was also observed. This change is neither significant nor out of the normal limits of the creatinine values (60 to 110 mmol/L) (19). Moreover, the creatinine level is correlated to the muscular mass, varied from men to women and may temporarily increase in case of dehydration, low blood volume, over-tiredness, lack of rest, dietary meat, drugs including cephalosporins, barbiturates and chemotherapeutic agents etc.

At the end of the treatment, a significant increase of the cholesterol level was observed (5.2 mmol/L from the beginning of the treatment to 6.4 mmol/L at the end). Such increase is not easy to attribute only to the drug effect since high cholesterol levels could be connected with saturated fat and cholesterol coming from animals (such as meats, whole milk, egg yolks, butter etc.), age, gender, some diseases, genetic factor etc. Furthermore, being overweight or taking some medicines may raise triglyceride levels.

In the assessment of the liver function enzymes, a slight and progressive decreasing of the values of ASAT and total bilirubin were observed during the treatment. The Alanine amino transaminase (ALAT) values of the beginning (7.4 UI/L) and the end (6.5 UI/L) of the treatment changed slightly whereas the Aspartate aminotransferase (ASAT) was significantly higher after 6 weeks of the treatment (from 7.4 to 12.5 IU/L). However, from week 6 to week 12, a significant decrease of ASAT was also observed (from 12.5 to 7.6 IU/L). Noteworthy, all the bilirubin, ASAT and ALAT values remained within the reference normal ranges of < 20 mmol/L, 5 – 35 IU/L and 5 – 30 IU/L, respectively (19).

As suggested by Malviya *et al.* (2010) for antidiabetic plants (2), the antihyperglycemic effect of *E. lecardii* may be attributed to the ability of its constituents to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. The crude extract of *E. lecardii* must contained a myriad of compounds that may be acting synergistically. During the past few years some of the new bioactive drugs isolated from plants showed antidiabetic activity with more efficacy than oral hypoglycemic agents used in clinical therapy. Many kinds of natural products, such as terpenoids, alkaloids, flavonoids, polysaccharides, phenolics, and some others such as guanidine derivative, steroid glycosides, peptides and amines have shown antidiabetic potential (14-15; 20).

The administration of 5g x 3 daily (teabag) of the leave of *E. lecardii* for 12 weeks, significantly ( $p \leq 0.05$ ) decreased the level of glycaemia without significant side effects or negative incidence on the kidney and hepatic markers. These findings supported the traditional antidiabetic use of the plant. Accordingly, *E. lecardii* can be very useful as medicinal agent in ameliorating health problems such as *diabetes mellitus*. These data need to be confirmed in a standard double blinded clinical trial. The isolation and identification of the constituents of the plant are in progress.

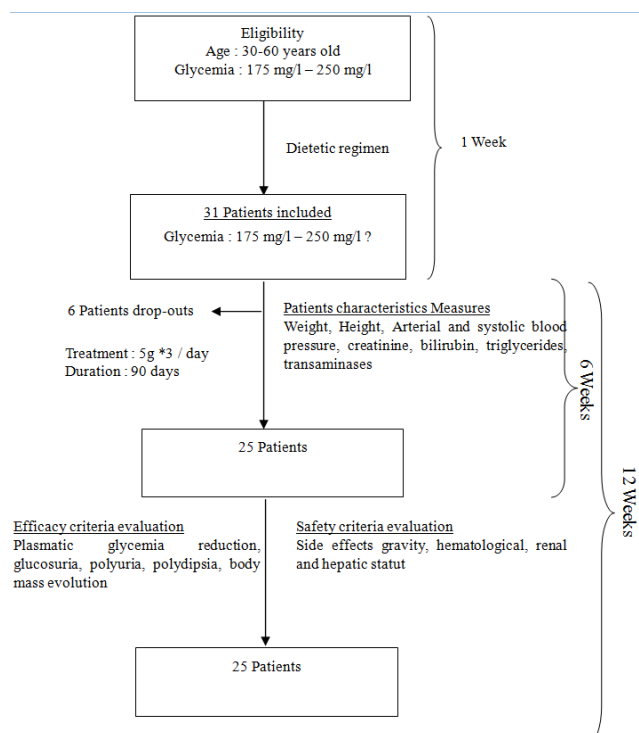


Figure 1. Patients flow chart

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