

Benabdelkrim I¹, Rachid A¹, Zaid A^{1*}, Cherrah Y², Alaoui T¹, Guéant JL³, El Badaoui K¹

¹ University of Moulay Ismail, Faculty of Sciences, Meknes, Morocco.

² Faculty of Medicine, Department of Pharmacology, Rabat, Morocco.

³ Faculty of Medicine, Nancy, France.

Abstract

The aqueous extract of *E. centaurium*, administered to merione at 200 mg/kg for 6 months produced a significant reduction in glycemia, insulinemia, fructosamine and glycosylated haemoglobin. It also exhibited an important decrease of lipidic parameters such as cholesterol, LDL-cholesterol, triglycerids. The results showed no significant diminution of the weight.

Keywords: *Erythrea Centaurium*; Meriones; Insulino-Resistance; Cholesterol; HDL; LDL; Triglycerids; Glucids and Lipids Metabolism.

*Corresponding Author:

Abdelhamid Zaid,

University of Moulay Ismail, Faculty of Sciences, Meknes, Morocco.

E-mail: zaid_abdel@yahoo.fr

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Introduction

Erythrea centaurium Rafn. (Gentianaceae) attracted our attention in view for its common use on the folk medicine. People also drink a decoction for treatment of diabetes mellitus, obesity, hypertension and other diseases such as gastritis and renal lithiasis. [1,2] There is general consensus that these metabolic disorders have hyperinsulinaemia and insulin resistance as common link leading to macrovascular and microvascular alterations. [3,4]

Among animal models used for studying metabolic diseases, Merione shawi (desert rodent) is an excellent one to spontaneously develop hyperinsulineamia, insulin resistance, hyperlipideamia and diabetes when captured. [5]

In spite of an extensive search, it was not possible to find more literature concerning the related pharmacological actions of *E. centaurium*. The present study is, therefore, undertaken to work out whether the aqueous extract of *Erythrea centaurium* exerts antidia-

betic and antihyperlipemic effects in merione shawi.

Experimental

Plant materiel. *Erythrea centaurium* is collected in July at the south of Moroccan Pré-Rif mountain and shade dried at room temperature.

2 g of *E. centaurium* aerial parts were soaked for 10 min in 100 ml of distilled water then administered by gavage once a day at rate of 200 mg of dried plant by kg of body weight for 6 months.

Animal. The *merione shawi* used in our experiment were devastating rodents of the family of Gerbillidae. They were gathered in the Moroccan desert and housed in the laboratory's animal house at constant temperature of 25°C and 12h light-dark cycle.

Our study used 20 male and female merione submitted to standard diet and water *ad libitum* for 6 months.

The animals were divided into two groups:

- The control group (n=10) was given oral administration of a placebo.
- The treated group (n=10) received the aqueous extract.

Biochemical analysis

Blood samples were taken from retro orbital sinus in fasted animals

Glucose and insulin measurements: Plasma glucose was measured using glucose oxidase (PAP 250 Glucose oxydase AMES-MILES). [6] Plasma insulin concentration was measured on samples stored at -20°C by radioimmunoassays (INSIK-5 P2796. DIASORIN). [7]

Fructosamine method used a reducing properties of the fructosamine in alkaline middle and glycated polylysine as calibrator. [8]

Glycosylated haemoglobin is a specific dosage of the haemoglobin by HPLC from 4th month of treatment. [9]

Plasma lipids: HDL-cholesterol, and LDL-cholesterol were dosed by precipitation, cholesterol and triglycerids dosed by enzymatic method (KIT AMES - MILES). [10,11,12] Values of weight have been measured monthly.

Statistical analysis: Data were expressed as the mean \pm S.E.M, and the Student's t-test was used to evaluate the significance of the results.

Results

As results showed the control group of merione shawi exhibited elevated fasting plasma glucose (13.5 ± 0.5 mM) (Figure. 1) and an increase of plasma insulin ($250 \mu\text{U/ml} \pm 10$ to $260 \mu\text{U/ml} \pm 0.9$) (Figure. 3). Moreover, lipid metabolism was characterized by enhanced plasma levels of triglycerids (1.50 ± 0.25 mM), total cholesterol (2.85 ± 0.45 mM) and LDL cholesterol (1.30 ± 0.10 mM).

After 6 months, the control group showed an important increase of insulin levels (Figure. 3) and plasma glucose rate (Figure. 1).

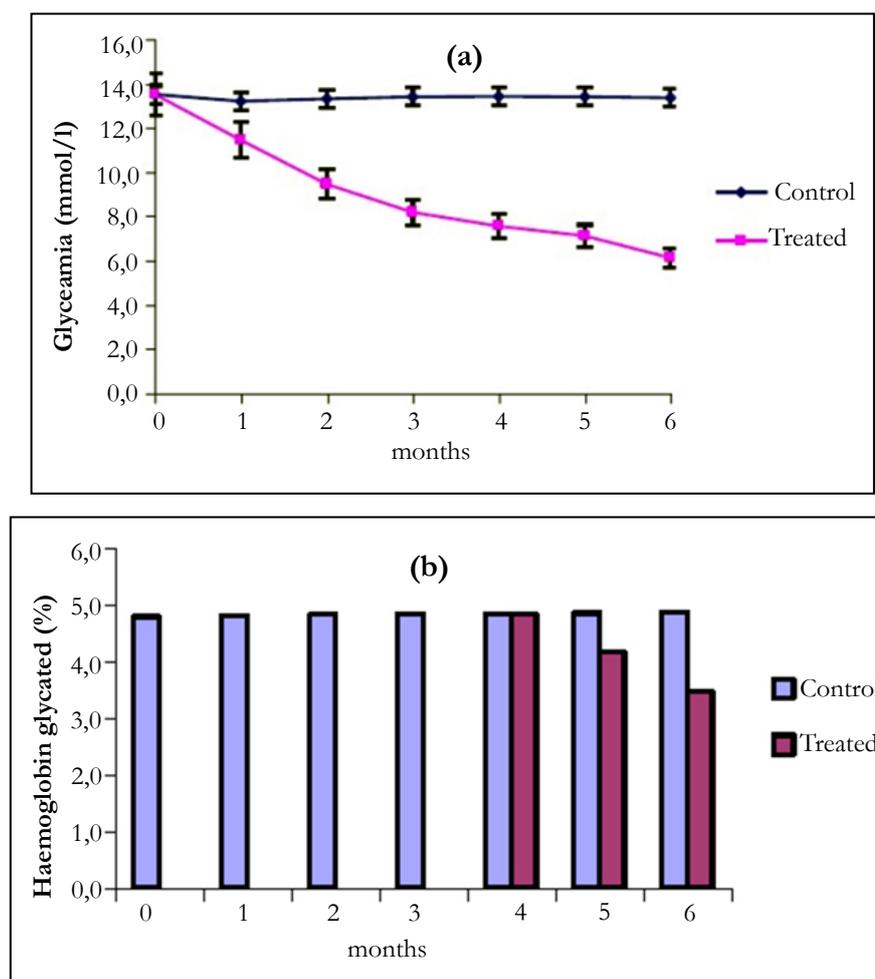
Thus parameters induced an increase of glycated haemoglobin (4.87 ± 0.28) (Figure. 1) and fructosamin (1.95 ± 0.12 mM) (Figure. 1). The lipid parameters such as total cholesterol, triglycerids and LDL cholesterol increased while HDL cholesterol decreased (1.20 ± 0.2 mM to $1.50 \text{ mM} \pm 0.02$ mM) (Figure. 2).

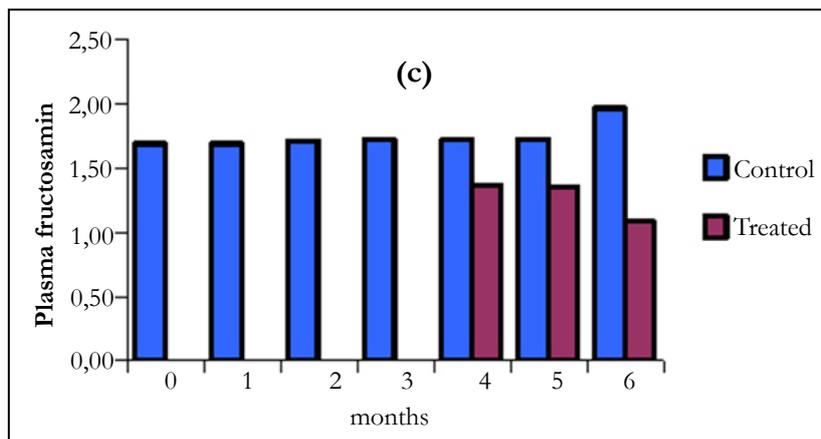
In the first month of treatment, the treated merion with *E. centaurium* extract exhibited an important decrease in plasma level of glucose (C: 13.20 ± 0.50 mM vs. T: 11.44 ± 0.10 mM, $p < 0.05$) (Figure. 1). It became very significant 5 months after (C: 13.40 ± 0.69 mM vs. T: $7, 11 \pm 0.20$ mM, $p < 0, 01$) (Figure. 3). The plasma insulin level declined to values of $230 \pm 2 \mu\text{M/ml}$ (Figure. 9). These effects were associated with lowering of glycosylated haemoglobin rate (C: 4.85 %, T: 3.47 %, $p < 0.01$) and plasma fructosamin level (C: 1.95 ± 0.10 mM vs T: 1.07 ± 0.12 mM, $p < 0.05$) (Figure. 1).

However, no significant modifications were noted in body weight (Figure. 3).

The lipid parameters exhibited a significant decrease in plasma level of total cholesterol (C: 3.00 ± 0.20 mM vs T: 2.04 ± 0.06 mM, $p < 0.05$) (Figure. 2). The treatment also led to a decrease in fasting LDL cholesterol (C: 1.50 ± 0.05 mM vs T: 0.80 ± 0.04 mM) (Figure. 2). While HDL cholesterol plasma levels increased (C: 1.03 ± 0.06 mM vs T: 1.82 ± 0.01 mM) (Figure. 2). The results showed that the *E. centaurium* aqueous extract had a significant reducing effect on the plasma triglycerids (C: 2.50 ± 0.30 mM vs

Figure 1. Effects of Erythrea centaurium aqueous extract on (a) plasma fasting glucose, (b) haemoglobin glycosylated and (c) plasma fructosamin in merione shawi





Significant difference from control rats * p<0.05 and ** p<0.01

Figure 2. Effects of Erythraea centaurium aqueous extract on (a) plasma total cholesterol, (b) HDL cholesterol and (c) LDL cholesterol levels in merione shawi

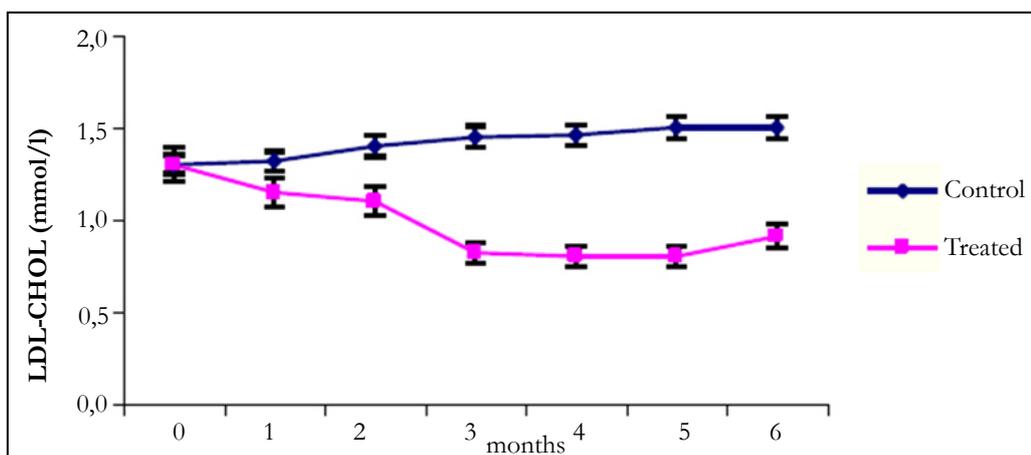
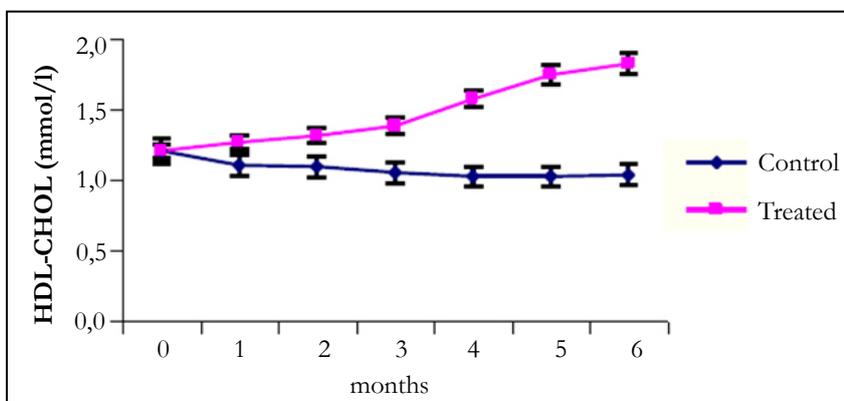
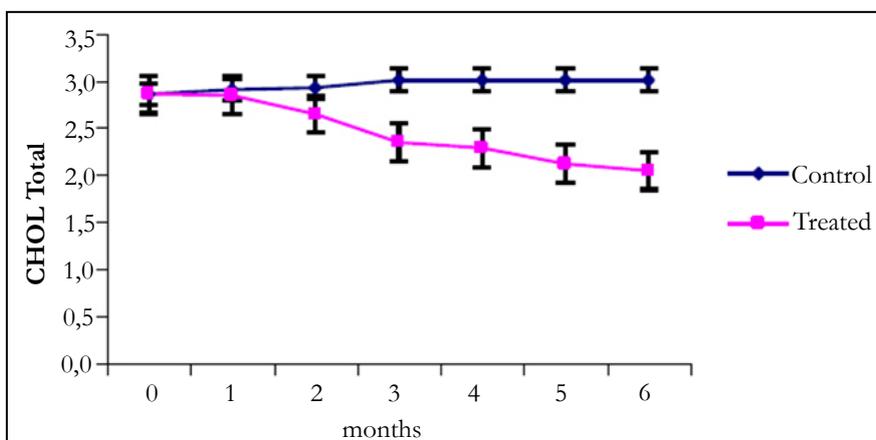
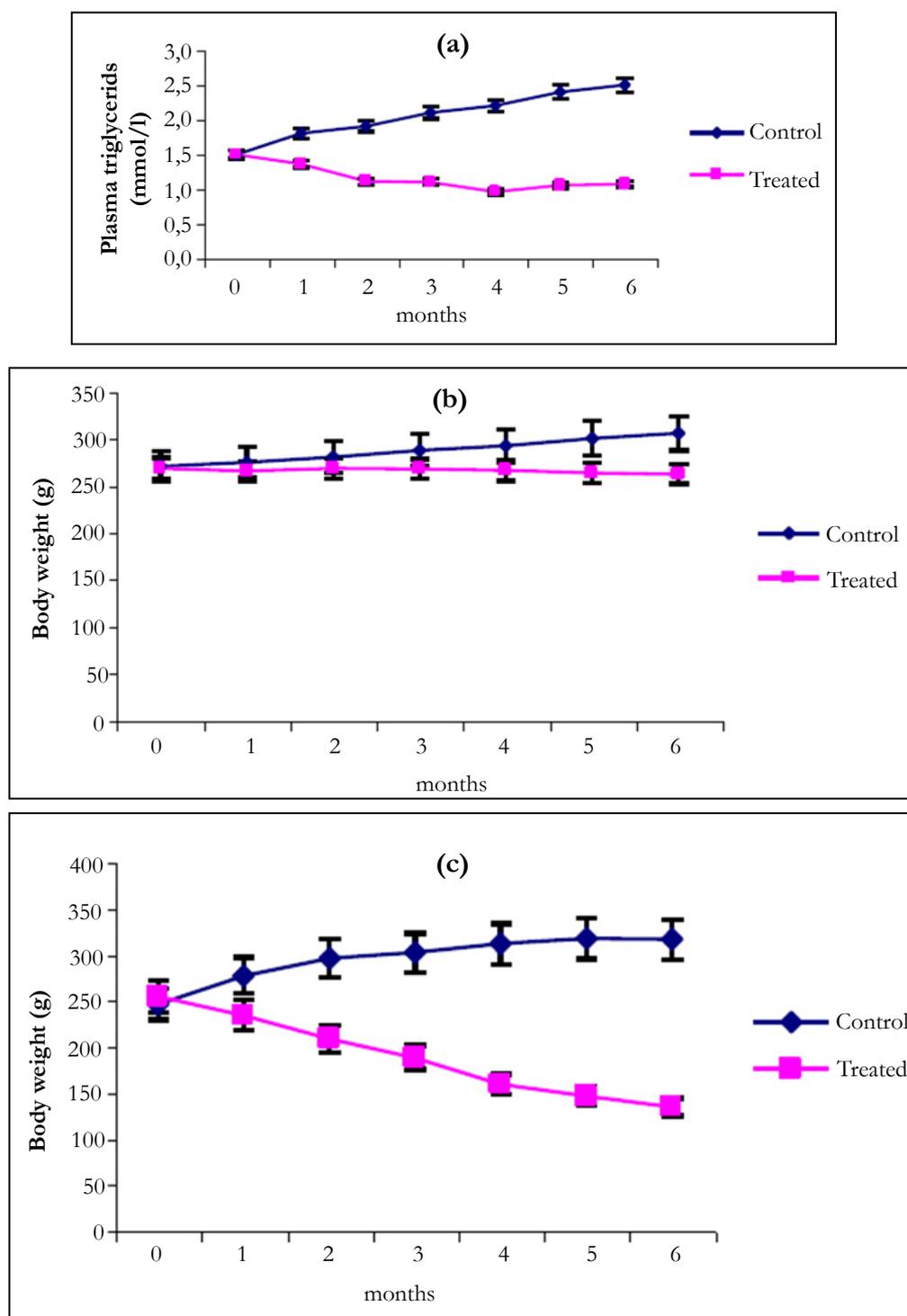


Figure 3. Effects of *Erythraea centaurium* on (a) plasma triglycerids, (b) body weight and © plasma insulin

T: 1.04 ± 0.09 mM, $p < 0.05$) (Figure. 3).

Discussion

The data obtained in the present study showed that Merione shawi on the captivity develops a diabetes mellitus and dyslipidemia. They had elevated fasting plasma levels of glycaemia, insulin, triglycerids, total cholesterol and LDL cholesterol. These results confirm the anterior investigations about major disturbances in carbohydrate and lipid metabolism in Merione shawi. [5,28]

Treatment with *E. centaurium* aqueous extract markedly reduced the unbalanced glucose lipid metabolism. It is very clear that this can treatment exhibits significant hypoglycaemic and antihyper-

glycaemic activity when given orally. The results are in agreement with results obtained on alloxan induced diabetic rats and normoglycaemic rats treated by aqueous extract of *E. centaurium* [13,14,15]. The crude extract exhibits no toxicity that testifies a common use on the Moroccan folk medicine [16].

On the basis of our experimental work, it appears that dried plant of *E. centaurium* cause a decrease in the concentrations of blood glucose and a reduction in the percentage of glycosylated haemoglobin and fructosamin in diabetic merione. Because it was a correlation between these parameters and glucose regulation in diabetes mellitus. It also reflects the carbohydrate status of the diabetic patients [17]. Previous investigations using hypoglyca-

mic plants suggest that this activity may result from at least one of the following mechanisms: potentiation of glucose induced insulin release [18], inhibition of intestinal absorption [19], increase of peripheral glucose uptake [20], and/or reduction or inhibition of hepatic glycogenolysis and neoglycogenesis or an increase of hepatic glycogenesis. [21,27]

According to the plasma insulin levels and the observations in diabetic rats induced by alloxan, it is suggested that the decoction of *E. centaurium* acts by extrapancreatic mechanism.

The lipid metabolism was also seriously affected, cholesterol metabolism in particular was characterized by increases in LDL but very limited increase in HDL cholesterol.

Treatment with *E. centaurium* crude extract markedly reduced total cholesterol, LDL cholesterol, led to a decrease in lipid peroxidation capacity, lowered plasma fasting glucose. The decrease in plasma insulin observed in treated animals proved that the plant may be act by a peripheral insulin-like mechanism.

The causality of metabolic disorders is largely controversial but experimental and clinic arguments suggest that the diabetic state associated to the obesity and to the dyslipidemia is intimately linked to an insulino-resistance. [22,23,24,25]

The earlier studies showed that *E. centaurium* contains several components which can be responsible for the antidiabetic and antihyperlipimiant effects [26]. Nevertheless, the mechanism of the action of the extract remains again to elucidate.

Conclusions

On the basis of the obtained results, the merione shawi in captivity can develop hyperglycaemia, hyperinsulinemiae and hyperlipidemia. These characteristics make merione shawi an ideal model for studying unbalanced lipid and carbohydrate metabolism and in addition for investigating the possible therapeutic effects.

Treatment with the aqueous extract of *Erythrea centaurium*, administered to reason 200 mg/kg correct the hyperglycemia of the meriones by decreasing plasma glucose and insulin values. The consequently, the phenomenon of glycation is reduced, and induced an important diminution of fructosemia. It proves also the antihyperglycemic effect of *Erythrea centaurium*.

Furthermore, the administration of the crude extract has the tendency to decrease the lipid components which explain the hypolipimiant effect of *Erythrea centaurium*. However, further studies are needed to isolate and elucidate the active chemical constituents as well as to investigate the plant as a potential source of new antidiabetic and antiobesity drugs.

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