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Research Article

Effects of Aqueous Extract of *Launaea taraxacifolia* Leaf on Glucose, Glycogen Levels and Lactate Dehydrogenase Activity in Male Wistar Rats

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Abstract
Launae taraxacifolia is an annual West Tropical Africa herb commonly known as wild lettuce. The leaves of *Launae taraxafolia* (*L.taraxafolia*) have been reported to possess traditional, medicinal and social uses but little has been reported of its effect on blood glucose level. This study was therefore designed to determine the effect of aqueous extract of *L. taraxacifolia* leaf on blood glucose, liver and muscle glycogen levels and lactate dehydrogenase activity (LDH) in rats. Forty (40) adult male rats were divided into eight groups of 5 rats per group (n=5). Groups I, II and III rats were administered orally with 100 mg/kg, 200 mg/kg and 500 mg/kg doses of aqueous extract of *L. taraxacifolia* leaf for one week while rats in groups V, VI and VII received same doses of the leaf extract for 2 weeks. The control groups were given distilled water. Blood glucose was determined by modified glucose oxidase method. Liver and muscle glycogen content was estimated by anthrone reagent method while the LDH activity was measured using commercial LDH Randox kits. The results showed that the 100 mg/kg, 200 mg/kg and 500 mg/kg doses of the aqueous leaf extract caused significant decrease ($P<0.05$) in blood glucose levels of rats after 1 week of treatment but did not produce any significant effect on glucose levels after 2 weeks of treatment. However, after 1 week of treatment, the 200mg/kg dose of the extract caused significant increase in muscle glycogen, LDH activity but significant reduction in liver glycogen while the 200mg/kg did not cause any effect on liver glycogen, muscle glycogen and LDH activity after 2 weeks of administration. This study has shown that *L. taraxacifolia* leaf has glucose lowering effect and may be acting through glycolysis and glycogenesis in the muscle.

Key words: Glucose, glycogen, *Launaea taraxacifolia*, lactate dehydrogenase activity

INTRODUCTION

The use of herbal products for medicinal benefits has played a significant role in nearly every culture on earth. Herbal medicine was practiced by ancient people of Africa, Asia, Europe and the Americas (Wargovich *et al*., 2001). Over 50% of all modern clinical drugs are of natural product origin. Natural products play an important role in drug development programs of the pharmaceutical industry.

L. taraxacifolia is an annual West Tropical Africa herb commonly known as wild lettuce. The plant is known in French as langue de vache which implies tongue of the cow. There are some common names of the plant; Ga; agblòke, Ewe (anlo); aŋòto, Twi; dadedru, Akan Akuapem; nnenoa (boil today) Hausa; namijindayi (applied loosely) Yoruba; efoyanrin, Sierra Leone-Kissi; bekuhoa-pomboe. *L. taraxacifolia* is used locally as a remedy for prevention and treatment of measles and diabetes mellitus. It has been reported to possess hypolipidaemic effect (Ayensu, 1978, Adebisi; 2004; Obi *et al*., 2006). The leaves of *L. taraxacifolia* are used to stimulate lactation in nursing cows and induce multiple births in sheep and goats (Wichtl, 1994). Phytochemical screening revealed that the leaf contains flavonoids, saponin, phenol, oxalate, tannins, phytate, ascorbic acid and minerals such as Calcium, potassium, magnesium, zinc, manganese, selenium (Arawande *et al*., 2013). Previous studies have also reported the antioxidant activity of *L. taraxacifolia* due to the presence of flavonoids, phenol and ascorbic acid (Gbademosi *et al*., 2012; Oduse *et al*., 2012; Arawande *et al*., 2013). The presence of these phenolic metabolites in the L. taraxifolia leaves protect against free radical mediated diseases such as Alzheimer's, cardiovascular diseases and cancer (Cartea *et al*., 2011). Anti-clastogenic effects of launaea taraxacifolia leaf extract on cisplatin-induced micronuclei in bone marrow erythrocytes and how it ameliorates cisplatin-Induced Hepato-renal Injury and testicular dysfunction has also been reported (Adejuwon *et al*., 2014). Literature is scarce on the effect of *L. taraxacifolia* on blood glucose levels.

Enyonamkuatsienu (2012) reported the safety assessment of the leaf extract in rodents without adverse effect on the blood, liver and a possible reno-protective action. The cytotoxicity, antioxidant and hypolipidemic effects of *Launaea taraxacifolia* leaf extract on Cell Lines HepG2 and PLB985 was also reported (Koukoui *et al*., 2015). Recently, Owoeye and Malomo (2015) in their study showed the protective effects of *L. taraxacifolia* leaf extract against radiation-induced haematological, behavioural and alteration of microanatomy of rat cerebellum and hippocampus and chemo protective effects against cisplatin-induced oxidative stress, neuronal death and alteration of microanatomy of rat brain (Owoeye *et al*., 2015).

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There is little information on the effect of *Launaea taraxacifolia* on blood glucose levels therefore, this study was designed to determine the effects of L .taraxacifolia leaf on blood glucose, glycogen levels and the possible mechanism of its effects on blood glucose in the rats.

MATERIALS AND METHODS

Forty (40) adult male wistar rats obtained from the Central animal house, Department of Physiology, College of Medicine were used for the study. The rats housed in well-ventilated plastic cages were provided with rat pellets and water ad libitum. The rats were randomly divided to eight groups of 5 rats per group (n=5). Groups I, II, III, IV rats were given orally 100 mg/kg, 200 mg/kg, 500 mg/kg doses of aqueous extract of *L. taraxacifolia* and distilled water for 1weekrespectively while animals in groups V, VI, VII, and VIII received orally 100 mg/kg, 200 mg/kg, 500 mg/kg doses of same aqueous extract of *L. taraxacifolia* and distilled water for 2 weeks respectively.

Selection and preparation of aqueous extract of *L. taraxacifolia* : The fresh leaves of *L. taraxacifolia* were obtained from the popular Bodija market in Ibadan, Nigeria and authenticated by forest herbarium of the Forest Research Institute of Nigeria, Ibadan (FRIN) with voucher number FHI-110145.

The leaves (300grams) were air-dried for 4days, powdered and soaked in 4litres of distilled water heated at a sustained temperature of 60oC for 24 hours after which they were filtered using filter papers. The filtrate was concentrated under reduced pressure at 40oC using a rotary evaporator to give 83.5g residue, a yield of 27.8%. (Amir *et al*., 2005). The administered dose was then calculated per kilogram body weight of the rats

Determination of blood glucose and glycogen contents: The fasting glucose level was determined after 7 and 14 days of administering the aqueous extract of *L. taraxacifolia* leaves to the animals. The blood glucose was determined using modified glucose oxidase method (Trinder, 1969). Liver and muscle (gastrocnemius) glycogen content was estimated by anthrone reagent method (Seifter *et al*., 1950; Jermyn, 1975).

Lactate dehydrogenase (LDH) estimation: The LDH activity was determined using a commercial LDH Randox kit from Ranndox Laboratory Limited, United Kingdom. Blood serum was used as the sample, mixed with appropriate volume of the reagent; the absorbance was then read at 340/nm. Calculation was done using:

U/L = 4127* Δ A 340nm/min.

Principle: Pyruvate + NADH + H+ $\xrightarrow{\text{LD}}$ L-lactate + NAD+

Statistical analysis

All values given are mean ± S.E.M of the variables measured. Values between two groups were compared using students' -test and values of $P<0.05$ were considered statistical significant.

RESULTS AND DISCUSSION

The blood glucose, glycogen levels and lactate dehydrogenase (LDH) activity in rats treated with aqueous extract of *L. taraxacifolia* leaf for 1 and 2 weeks are shown in tables 1 and 2 respectively.

The three doses (100 mg/kg, 200 mg/kg and 500 mg/kg) of aqueous extract of *L. taraxacifolia* leaf caused significant decrease in blood glucose level after 1 week treatment compared to control. Also, the 200 mg/kg of the extract caused significant increase in muscle glycogen, lactate dehydrogenase activity and significant reduction in liver glycogen after 1 week treatment compared with control (Table 1). However, after two weeks of treatment, the three doses (100 mg/kg, 200 mg/kg, and 500 mg/kg) of *L. taraxacifolia* leaf extract did not produce any significant change in blood glucose, glycogen levels and lactate dehydrogenase activity compared to the control (Table 2).

The results of the present study showed that the three doses (100 mg/kg, 200 mg/kg, and 500 mg/kg) of aqueous extract of launea taraxacifolia leaf caused significant decrease in blood glucose levels after 1 week of administration. The glucose lowering effect of *L. taraxacifolia* leaf extract may be due to the presence of flavonoids, phenol, tannin, saponin, phytate, ascorbic acid and other nutrients as reported by (Arawande *et al*., 2013; Adinortey *et al*., 2012). This is consistent with previous studies (Akah and Okafor, 1992; Adeneye and Agbaje, 2008; Narender *et al*., 2011; Momoh *et al*., 2011) that plants containing phenolic compounds and other metabolites possess hypoglycemic, hypotensive and other pharmacological properties (Oladele *et al*., 1995; Sudheesh *et al*., 2005). The glucose removed from the blood may have gone through glycolytic pathway to produce pyruvate or lactate or converted to glycogen.

Table 1:
Effects of one-week administration with aqueous extract of *L. taraxacifolia* leaf on blood glucose, liver glycogen, muscle glycogen and lactate dehydrogenase (LDH) activity.

	Control	100 mg/kg	200 mg/kg	500 mg/kg
Blood glucose mg/dl)	82.8 ± 2.22	71.2 ± 2.63*	70.2 ± 3.24*	63 ± 1.7*
Liver glycogen (mg/100g tissue)	23.89 ± 1.36	25.28 ± 4.44	13.57 ± 1.94*	22.54 ± 2.85
Muscle glycogen (mg/100g tissue)	77.55 ± 4.2	79.68 ± 4.7	100.93 ± 5.27*	75.46 ± 3.7
LDH (U/L)	22.69 ± 2.66	15.47 ± 1.97	46.75 ± 4.24*	28.88 ± 2.91

* $P<0.05$ when compared with control group

Table 2:
Effects of two weeks administration with aqueous extract of *L. taraxacifolia* leaf on blood glucose, liver glycogen, muscle glycogen and lactate dehydrogenase (LDH) activity.

	Control	100 mg/kg	200 mg/kg	500 mg/kg
Blood glucose (mg/dl)	64.2 ± 4.97	54.2 ± 2.95	54 ± 2.54	52.6 ± 2.3
Liver glycogen (mg/100g tissue)	10.32 ± 2.95	12.33 ± 3.46	11.04 ± 2.31	9.07 ± 1.21
Muscle glycogen (mg/100/g tissue)	164.56 ± 13.14	234.6 ± 14.93*	182.98 ± 9.06	161.03 ± 6.19
LDH (U/L)	33.01 ± 8.42	27.85 ± 6.61	36.11 ± 7.41	48.49 ± 6.38

* P<0.05 when compared with control group

It is interesting to note that the 200mg/kg dose of aqueous extract of *L. taraxacifolia* leaf did not only cause reduction in blood glucose level but caused significant increase in muscle glycogen, LDH activity and significant reduction in liver glycogen. The observed increase in muscle glycogen caused by 200/mg/kg dose of leaf extract in the present study seems to suggest that the glucose removed due to glucose lowering effect of *L. taraxacifolia* must have been taken up by muscle tissue to form muscle glycogen. This may be responsible for the increased muscle glycogen observed in the present study. This is probably the mechanism by which *L. taraxacifolia* leaf extract lowers blood glucose level and may be mediated through insulin release (Chakrabartiet *et al*., 2003). Although we did not measure insulin in this study it is recommended for further study. Furthermore, it has been reported that flavonoids can influence glycogen deposition in different tissues as well as interact with key enzymes of the glycolytic route in rats (Ferrer *et al*., 2003; Park *et al*., 2006).

The significant increase in LDH activity observed in the present study seems to suggest that part of the glucose removed due to glucose lowering effect of the leaf extract may have gone through the glycolytic pathway to produce pyruvate and lactate. The lactate thus produced may be converted back to glucose through gluconeogenesis. This is part of the mechanism to increase the blood glucose back to normal. A balance between hepatic gluconeogenesis and peripheral glycolysis is an important homeostatic function. Lactate dehydrogenase activity catalyzes the interconversion of pyruvate and lactate (Gerhardt-Hansen, 1968). Lactate is an active metabolite that can move between cells, tissues, and organs where it may be oxidized as a fuel or converted to form pyruvate or glucose (Andrew *et al*., 2005).

The same 200 mg/kg of the extract caused significant decrease in liver glycogen probably through glycogenolysis. This is a compensatory mechanism to raise the glucose level back to normal. However, after two weeks of administration of the leaf extract there was no significant change in blood glucose, liver and muscle glycogen and LDH activity. This could be due to homeostatic mechanism of the body to balance the significant glucose reduction observed after one week probably through stimulation of counter regulatory hormones like glucagon, cortisol and epinephrine. Measurement of these hormones involved in glucose metabolism will provide better understanding of the mechanism by which *L. taraxacifolia* leaf extract lowers blood glucose. These observations thus suggest that the *L. taraxacifolia* leaf lowers blood glucose level probably through glycogenesis and glycolysis in the muscle while the homeostatic mechanisms through glycogenolysis and gluconeogenesis in the liver try to restore the blood glucose level back to normal.

In conclusion, the results of this study have shown that *L. taraxacifolia* leaf has a glucose lowering effect. The possible mechanism by which *Launaea taraxacifolia* leaf brings about this effect may be through glycogenesis and glycolysis in the muscle

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