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ANTIDIABETIC EFFECTS OF *Newboldia laevis* (P. Beauv) METHANOL LEAF EXTRACT ON ALLOXAN INDUCED DIABETIC RATS

Bosha J. A[1] Anaga A.O[2] and Asuzu, I. U[2]

1Department of Veterinary Physiology and Pharmacology, University of Agriculture, Makurdi, Benue state, Nigeria.

2Department of Veterinary Physiology and Pharmacology, University of Nigeria, Nsukka, Enugu state, Nigeria.

Corresponding Author: Bosha J. A; Email: boshajoel@yahoo.com; phone no: +2347031320514,

Abstract

Diabetis mellitus (DM) is a chronic metabolic disease that affects both man and animals. The high prevalence rate of DM and its attendant high cost on healthcare have necessitated search for cheaper, effective and readily available alternatives in plants. One of such plants used in Nigeria and other African countries is Newbouldia laevis (P. Beauv) (NLE). This work examines the effects of Newbouldia laevis on alloxan- induced diabetes in albino rats. The result showed that NLE has dose- and time-dependent antidiabetic effect. The lowest dose (62.5 mg/kg) reduced the fasting blood sugar (FBS) by 0, 0.91, 7.04, and 40.1 % 0n days 0, 7, 14 and 21 respectively, while the highest dose (250 mg/kg) reduced the FBS by 0, 13.23, 21.37, and 67.46 % on days 0, 7, 14 and 21 respectively. Meanwhile, glibenclamide reduced the FBS by 0, 37.87, 36.10 and 70.20 % respectively within the same period. The untreated group (10 ml/kg distilled water) showed an increase in the FBS by 0, 1.7, 7.1 and 21.99 % on days 0, 7, 14 and 21 respectively. The body weight of the rats showed a decrease between 3.1- 8.9 % in the untreated group of rats. NLE on the other hand showed a slight increase in body weight that ranges between 3.03-15.91% just like glibenclamide which showed an increase between 4.06-10.57 %. At the end of 21 days, there was no significant ($p > 0.05$) difference between the NLE and glibenclamide treated groups. This then shows that NLE has dose- and time –dependent antidiabetic effect which is likely similar to glibenclamide and its folkloric usage has pharmacological basis.

Keywords: Alloxan, antidiabetic, diabetes, *Newbouldia laevis*, rats.

Introduction

Diabetis mellitus (DM) is a chronic metabolic disease in which the body does not produce and or properly utilize insulin, as a result there is chronic hyperglycemia due to disturbances in carbohydrate, fats and protein metabolism (Khan,2010). DM affect man and several other animals including dogs, cats, sheep, cattle, horses, pigs and virtually all laboratory animals and non-human primates (Khan, 2010). The high prevalence rate of DM and its attendant high cost on healthcare have necessitated search for cheaper, effective and readily available alternatives in plants (Evans, 2009). The universal role of plants in the treatment of diseases, and the source for many pharmaceuticals today has been acknowledged through out history (Wagner and Ulrich, 2009). One of such plants used in Nigeria and other African countries is *Newbouldia laevis* (P. Beauv) (NLE). Its ethnic names include "Aduruku" or 'Bareshi" in Hausa, "Ogirisi" in Igbo, "Akoko" in Yoruba, "Kontor" in Tiv. In Ivory Coast it is called "Sokunde" and it is known as "Sesemasa" in Ghana (Keay, 1989; Burkil, 1994). The English common name is "Border" or "Boundary" tree. The aim of this work was therefore, to investigate the anti- diabetic effects of methanol leaves of *Newboldia laevis* on Alloxan -induced diabetic rats in order to establish the pharmacological basis for its folkloric use in the treatment of Diabetes mellitus with a view of isolating and identifying the active anti-diabetic principle(s) responsible for such anti-diabetic activities.

Materials and Methods

One (1 kg) of the leaves of *Newbouldia laevis* (NLE) were collected and identified by Mr. Terry Waya with a specimen number UAM/FHM/205 deposited at the Forestry hebarium at the University of Agriculture, Makurdi. The leaves were grinded and extracted by cold maceration using 80% aquous methanol. Rotary evaporator (Rotavapor-R-215) was used to concentrate and dry the extract *in vacuo* and the percentage yield was calculated. Diabetes was induced by single intraperitoneal administration of alloxan monohydrate (Sigma) at the dose of 150 mg/kg in 15 h fasted male albino rats (Szudelski, 2001). The fasting blood sugar (FBS) level was measured with Accu- check advantage II® (Roche Diagnostics) every other day. Rats with FBS greater than or equal to (≥) 7.0 mmol/L were

selected for the experiment. The 40 rats were randomly divided into five groups (n=8).Groups 1,and 2 were given 10 ml/kg of distilled water and 2 mg/kg of glibenclamide (Sigma) respectively, while groups 3, 4 and 5 were given the extract in this order 62.5, 125.0, and 250.0 mg/kg of the extract respectively .All treatments were given orally by intragastric tube for 21 days. The FBS and body weights of the rats were taken at days 0, 1, 7, 14 and 21. Food and clean tap water were administered *ad libitum* except on the days the FBS was to be taken in which the rats were fasted for 15 h.

Result and Discussion

The universal role of plants in the treatment of diseases, and the source for many pharmaceuticals today has been acknowledged throughout history (Wagner and Ulrich, 2009). In view of the above facts, the World Health Organization (WHO) has recognized the role of herbal, traditional or alternative/complementary medicine in primary health care, especially in developing countries and has encouraged member nations to develop national policies for proper identification, sustainable exploitation, scientific development and appropriate utilization of herbal medicines appropriate for their situations, considering the fact that the use of medicinal plants is the most common form of traditional medicine world wide (WHO, 2005). Newbouldia has been used in Africa to treat diabetes and many other disease conditions for times immemorial (Burkil,1994). The ability of NLE to reduce the fasting blood sugar (FBS) of rats was tested as a means of evaluating its antidiabetic activity through a single intraperitoneal administration of 150 mg/kg of alloxan monohydrate. Fasting blood sugar (FBS) is a test of carbohydrate metabolism which measures blood glucose after a fast, which is usually 12-15 h. During this time, the body stimulates the release of the hormone glucagon which in turn releases glucose in to the blood stream through a catabolic process. Under normal circumstances, the body produces and processes insulin to counteract the rise in glucose levels, but in diabetes mellitus this process is impaired, and tested blood glucose levels remain usually high (Kaufman, *et al.*, 2009). In the present study, NLE at doses of 62.5, 125.0 and 250.0 mg/kg body weight caused significant ($p < 0.05 - 0.01$) dose and time-dependent decreases in the FBS levels of the alloxan-induced diabetic rats (Table 1). The lowest dose (62.5 mg/kg) reduced the FBS by 0, 0.91, 7.04, and 40.10 % 0n days 0, 7, 14 and 21 respectively. The middle dose (125.0 mg/kg) reduced the FBS by 0, 11.30, 14.43 and 56.0 % within the same period while the highest dose (250 mg/kg) reduced the FBS by 0, 13.23, 21.37, and 67.46 % on days 0, 7, 14 and 21 respectively. Meanwhile, glibenclamide the standard anti-diabetic agent reduced the FBS by 0, 37.87, 36.10 and 70.20 % respectively within the same period. The untreated group (10 ml/kg distilled water), rather showed an increase in the FBS by 0, 1.70, 7.10 and 21.99 % on days 0, 7, 14 and 21 respectively. The dose-dependent decrease of FBS in diabetic rats by *Newbouldia laevis* has been reported by other workers (Tanko *et al.*, 2008; Kolawole *et al.*, 2013, Bosha, 2015), though their period of administration of the extract was shorter. Herein we report the dose-and time- dependent antidiabetic effect of NLE. In DM there is high level glucose in the blood (hyperglycaemia) which is not able to be absorbed into the cells that needed them. The lack of absorption of glucose leads to hypoglycaemia at the cellular level while there is hyperglycaemia in the blood/plasma. The body now breaks down the stores of fats and proteins to make glucose and ketones in the liver and this result to loss of weight in both humans and other animals (Szudelski, 2001). The breakdown of protein and decreased protein synthesis lead to general lethargy, hypoalbulminia and decreased gamna globulins. The end result is negative energy balance, weight loss, increased susceptibility to infections and delayed wound healing (Umesh *et al.*, 2012). The extract (NLE) was able to inhibit the loss of weight in DM as shown in the reversal in loss of weight in all the NLE treated groups and glibenclamide. At the end of 21 days there was no significant ($p > 0.05$) difference between the NLE-treated groups of albino rats and the glibenclamide-treated rats. The effect amoung the NLE-treated groups on day 21 was somehow dose-dependent. This was not the case in the untreated group (Table 2). The untreated group showed consistent decrease (loss) in weight throughout the 21 days of the experiment. Weight measurement is used as an index to assess the severity and or response to treatment in type 1 diabetes (Mayfield, 1998). This also point to the fact that NLE was able to alter the pathophysiology of DM that normally leads to weight loss and negative energy balance.

Conclusion

In conclusion, it is established that *Newbouldia laevis* has dose- and time- dependent antidiabetic effects on alloxan -induced diabetes in albino rats. It also inhibit the wasting nature of DM by improving the body weight and negative energy

balance of the affected rats comparable to glibenclamide. Therefore its usage in folk medicine to treat DM has pharmacological basis.

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Table 1 : Percentage changes in FBS of rats administered NLE for 21 days (%)

Treatment	Day 1	Day 7	Day 14	Day 21
Dist H_20 10 ml/kg	0	+1.7	+7.1	+21.99
Glibenclamide 2mg/kg	0	_37.87	_36.10	_70.2
NLE(62.5 mg/kg)	0	_0.91	_7.04	_40.1
NLE(125.0 mg/kg)	0	_11.3	_14.43	_56.0
NLE(250 mg/kg)	0	_13.23	_21.37	_67.46

Table 2: Effect of NLE on mean body weight (%)

Treatment	Day 1	Day 7	Day 14	Day 21
Dist H_20 10 ml/kg	_7.1	_8.9	_3.1	_8.5
Glibenclamide 2mg/kg	4.06	+7.72	+10.57	+4.06
NLE(62.5 mg/kg)	_5.75	+15.09	+8.86	+3.03
NLE(125.0 mg/kg)	+2.71	+2.51	_0.33	3.25
NLE(250 mg/kg)	_7.07	+7.61	+15.91	+5.53

Key= + Increase in weight and FBS
_ Decrase inweight and FBS