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Alloxan-Induced Diabetes in Rats and the Effects of Black Caraway (*Carum carvi* L.) Oil on Their Body Weights

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Abstract: The effect of different doses of Black caraway (*Carum carvi* L.) oil on the body weights of alloxan-induced diabetic rats was studied. Forty white male albino rats of the Winster strain weighing between 145-240 g were used for this study. Diabetes was induced in the experimental rats with alloxan (70 mg kg^{-1} body weight). Group 1 rats served as the normal control, group 2 served as the caraway control, whereas group 3 rats served as the diabetic control. Groups 4, 5, 6, 7 and 8 were the test groups. All the test groups were administered various doses of the black caraway oil ranging from 5, 10, 20, 40 and 80 mg kg^{-1} body weights, respectively. Group 2 (the caraway control) rats were administered 10 mg kg^{-1} body weight of black caraway oil. The duration of the experiment was 10 weeks. The weights of the animals in each group were recorded daily throughout the duration of the experiment. The blood glucose levels in the different groups were assayed. The results show that the normal control, the caraway control and the diabetic rats treated with 10 mg kg^{-1} body weight of black caraway oil showed progressive and steady increase in the % mean weekly body weights, while the diabetic untreated rats and the other test groups showed decreasing and alternating increments, respectively in the % mean weekly body weights. The blood glucose level in the 10 mg caraway treatment group was significantly reduced ($p<0.01$) compared to the diabetic control and the other treatment groups. This shows that the black caraway oil increases the % mean weekly body weights of the diabetic/non-diabetic rats at a dose not more than 10 mg kg^{-1} body weight. It can also be inferred that the 10 mg kg^{-1} body weight of caraway oil is the safe dose that can be used in managing Diabetes mellitus. The information obtained from this study would be used in the management of diabetic patients.

Key words: Albino rats, alloxan, diabetes, treated, caraway oil, body weight

INTRODUCTION

Diabetes mellitus is a disease characterized by chronic hyperglycaemia and glucosuria produced by an absolute or relative insufficiency of insulin. The ailment may result into the development of further metabolic and anatomic disturbances among which is Lipemia, hypercholesterelaemia, loss of weight, ketosis, arteriosclerosis, gangrene, pathologic changes in the eye, neuropathy, renal disease and coma (Andrew *et al*., 2000; Swanston *et al*., 1990). Hyperglycaemia and glucose intolerance are common manifestations of several types of hormonal disturbances or imbalances, of which the most important is diabetes mellitus (Forster, 1987). This disease is the seventh leading cause of death in the world.

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Weight Loss which is one of the clinical features of diabetes mellitus may be due to the degeneration of the adipocytes and muscle tissues to make up for the energy lost from the body due to frequent urination and over conversion of glycogen to glucose. Weight loss is a very serious issue in the management of diabetes mellitus (Reno and Leland, 1999; Zink and Chafin, 1998).

The search for a cure for diabetes mellitus continues along traditional and alternative medicine. Many herbal supplements have been used for the treatment of diabetes, but not all them have scientific evidence to support their effectiveness (Morelli and Zoorob, 2000). Bitter melon (*Mormodica charantia*), Fenugreek and Soy beans have been studied as possible treatment in patients with diabetes, but the results of these were inconclusive or showed these products to be ineffective (Welinhinda *et al*., 1986; Madar *et al*., 1988; Librenti *et al*., 1992). This led to the study of many other plant products including Black caraway (*Carum carvi* L.) oil as possible treatment for diabetes mellitus.

The black caraway oil has been reported to have both hypolipidemic and hypoglycemic properties (Modu *et al*., 1997). Ene *et al*. (2006) reported that 10 mg kg^{-1} body weight of black caraway oil brought the hyperglycemic conditions of alloxan induced diabetic rats to normal. The caraway plant which is known scientifically as *Carum carvi* L. is indigenous to Europe and West Asia (Kocklar, 1981) and is now being cultivated in commercial quantity in Marte Local Government Area of Borno State, Nigeria. Chemical analysis reveals that the plant contains proteins, essential amino acids, phosphorus, calcium, potassium, magnesium, sodium, petroselinic acid and polyunsaturated fatty acid. The major fatty acids present are oleic and linoleic acid (A'bdel *et al*., 1993).

In the present study, the effects of different doses of black caraway oil were studied in alloxan-induced diabetic rats and its effects on their body weights were also studied.

MATERIALS AND METHODS

Forty white male albino rats of the Winster strain weighing between 145 and 240 g were used. The rats were randomly divided into eight groups of five rats each and maintained on a standard feed and water *ad libitum* throughout the experiment. Diabetes was induced in groups 3 to 8 rats by injecting them with 70 mg kg^{-1} body weight alloxan administered through the tail vein after fasting the animals for 24 h (Ajabnor and Tilmisany, 1988). The route of administration of alloxan is intraperitoneally. Diabetic condition was confirmed 24 h after alloxan injection. Not all the rats were diabetic at 24 h, but they were all found to be diabetic after 72 h.

Five milligrams, 10, 20, 40 and 80 mg kg^{-1} body weight of black caraway oil were then administered gastrointestinally by intubation to the test rats in groups 4 to 8, respectively. i.e, the route of administration of the caraway oil is oral. Group 3 rats served as the diabetic control. Group 2 rats which were non-diabetic were given 10 mg kg^{-1} body weight of black caraway oil (caraway control group), while group 1 rats served as the normal control. The body weights of the animals in all the groups were recorded daily throughout the duration of the experiment. Blood glucose levels were assessed in all the animal groups by using blood from the tail vein of the rats (Trinder, 1969). Two hours postprandial blood glucose and urine sugar tests were also conducted on the rats fortnightly to monitor the progress of their diabetic state. The experiment lasted for a period of 10 weeks.

The black caraway oil used for this study was obtained from Mecca in Saudi Arabia. This study was conducted between January and March, 2005 at the Biochemistry Department of University of Maiduguri, Nigeria.

All data generated were analyzed using Analysis of Variance (ANOVA).

RESULTS AND DISCUSSION

A general increase was observed in the level of blood glucose in the diabetic control rats (Table 1). This increase is statistically significant ($p<0.01$) compared to the normal control, normal rats

Table 1: Two hours postprandial blood glucose test (mmol L^{-1})

	0 week		4th week	
Groups	FBS	2HPP	FBS	2HPP
Group 1 (Normal Control)	6.72+0.67^{a}	7.21±0.96^{a}	6.51±0.72^{ab}	7.14±0.63^{ab}
Group 2 (Caraway Control)	6.81±0.58^{a}	7.74±0.96^{a}	6.01±0.35^{ab}	6.90±0.72^{ab}
Group 3 (Diabetic Control)	10.64±2.08^{b}	13.33±1.92^{b}	12.73±2.01^{bc}	12.91±1.95^{bc}
Group 4 (5 mg Rx group)	13.82±2.54^{c}	17.22±2.67^{c}	8.50±1.22^{ab}	10.12±1.94^{ab}
Group 5 (10 mg Rx group)	13.51±2.15^{c}	17.23±2.28^{c}	7.92±0.55^{ab}	7.95±1.35^{ab}
Group 6 (20 mg Rx group)	11.33±1.90^{c}	15.41±1.98^{c}	7.01±0.32^{ab}	7.35±0.60^{ab}
Group 7 (40 mg Rx group)	10.14±1.63^{c}	13.76±2.62^{c}	7.34±0.34^{ab}	10.12±1.02^{ab}
	8th week		10th week	
Groups	FBS	2HPP	FBS	2HPP
Group 1 (Normal Control)	6.00±0.42^{cd}	5.90±0.72^{cd}	5.64±0.44^{gh}	5.66±0.95^{gh}
Group 2 (Caraway Control)	4.81±0.62^{cd}	5.31±0.95^{cd}	4.78±0.54^{gh}	5.64±0.50^{gh}
Group 3 (Diabetic Control)	12.94±1.44^{ef}	18.72±3.35^{ef}	13.51±1.55^{ijk}	20.55±6.12^{ijk}
Group 4 (5 mg Rx group)	10.31±2.25^{ef}	16.20±3.12^{ef}	9.22±1.44^{lm}	13.21±3.01^{lm}
Group 5 (10 mg Rx group)	7.70±1.45^{cd}	9.66±2.45^{ef}	7.51±1.23^{gh}	9.00±1.85^{lm}
Group 6 (20 mg Rx group)	10.13±1.46^{ef}	12.31±2.15^{ef}	8.44±0.65^{gh}	10.66±1.04^{lm}
Group 7 (40 mg Rx group)	8.71±1.58^{cd}	10.41±1.66^{ef}	8.12±0.44^{gh}	9.91±1.55^{lm}

FBS = Fasting Blood Glucose, 2HPP = 2 h Postprandial, Values are mean ± standard deviation (n = 5), All groups were compared to each other at ($p<0.01$), Values with different superscripts vertically are statistically significant at ($p<0.01$)

fed with black caraway oil and the various groups of diabetic rats treated with the caraway oil. This increase which is as a result of the destruction of the beta cells of the pancreas by alloxan was brought to normal in the diabetic rats treated with 10 mg kg^{-1} wet weight concentrations of black caraway oil (Table 1). This is in agreement with the studies carried out by Ene *et al*. (2006).

Though no mechanism to the effect of black caraway oil on blood glucose has been proposed, it could be suggested that the oil might contain substances that mimic the action of insulin. It could be that the oil promotes utilization of blood glucose in the synthesis of fatty acids, since caraway oil contains medium chain fatty acids (Zink and Chaffin, 1998).

From the result of the urine sugar test (Table 2), the sugar was seen to disappear faster from the urine of the diabetic rats treated with 10 mg kg^{-1} body weight of black caraway oil compared to the other treatment groups. Sugar disappeared completely from the urine of the diabetic rats treated with 10 mg kg^{-1} body weight of black caraway oil at the 8th week, while traces of sugar were still present in the urine of the other treatment groups at same period of time. The disappearance of sugar from the urine of diabetic rats in the 10 mg kg^{-1} body weight caraway group at the 8th week concurs with the increment in weight at the same period of time. This could be explained by the fact that the glucose threshold level which was exceeded in the diabetic rats was brought to normal with 10 mg kg^{-1} body weight of black caraway oil compared to the diabetic and other treatment groups (Modu *et al*., 1997). During the course of this study ie from the 4th week of treatment, two rats each died in the 20 mg, 40 and 80 mg treatment groups, while none died in the other treatment groups. This death could be due to toxicity resulting from high dose of the caraway oil (Ene *et al*., 2006).

The normal control and the normal rats treated with black caraway oil showed increments in the percentage mean weekly body weights. The diabetic untreated rats showed drastic decrease in the percentage mean weekly body weights. The diabetic treated rats in 5, 20, 40 and 80 mg caraway treatment groups showed inconsistencies in their % mean weekly body weights, while the diabetic rats treated with 10 mg kg^{-1} body weight of caraway oil showed progressive and steady increase in their % mean weekly body weights (Fig. 1). This could be explained by protein sparing action i.e., gluconeogenesis from muscle protein (ketogenic amino acid) would result in decrease in total protein.

Table 2: Urine sugar test using Benedict's solution

Groups	4th weeks	8th weeks	10th weeks
Group 1 (normal control)			
$G1^1$	Nil	Nil	Nil
$G1^2$	Nil	Nil	Nil
$G1^3$	Nil	Nil	Nil
$G1^4$	Nil	Nil	Nil
$G1^5$	Nil	Nil	Nil
Group 2 (caraway control)			
$G2^1$	Nil	Nil	Nil
$G2^2$	Nil	Nil	Nil
$G2^3$	Nil	Nil	Nil
$G2^4$	Nil	Nil	Nil
$G2^5$	Nil	Nil	Nil
Group 3 (Diabetic control)			
$G3^1$	++++	++++	++++
$G3^2$	++++	++++	++++
$G3^3$	++++	++++	++++
$G3^4$	++++	++++	++++
$G3^5$	++++	++++	++++
Group 4 (5 mg Rx group)			
$G4^1$	++++	+	Nil
$G4^2$	++++	Nil	Nil
$G4^3$	++++	++	+
$G4^4$	++++	Nil	Nil
$G4^5$	++++	Nil	Nil
Group 5 (10 mg Rx group)			
$G5^1$	+++	Nil	Nil
$G5^2$	++	Nil	Nil
$G5^3$	+++	Nil	Nil
$G5^4$	++	Nil	Nil
$G5^5$	+++	+	Nil
Group 6 (20mg Rx group)			
$G6^1$	++	Nil	Nil
$G6^2$	+++	+	Nil
$G6^3$	+++	+	Nil
$G6^4$	-	-	-
$G6^5$	-	-	-
Group 7 (40 mg Rx group)			
$G7^1$	+++	+	Nil
$G7^2$	+++	Nil	Nil
$G7^3$	+++	Nil	Nil
$G7^4$	-	-	-
$G7^5$	-	-	-
Group 8 (80 mg Rx group)			
$G8^1$	+++	+	Nil
$G8^2$	+++	Nil	Nil
$G8^3$	+++	Nil	Nil
$G8^4$	-	-	-
$G8^5$	-	-	-

Rx = Treatment, G = Number of rats in a group, + = 50 mg, ++ = 100 mg, +++ = 150 mg, ++++ = 200 mg, - = Death, Nil = Negative

Since the oil has hypoglycaemic effect, this is expected hence the need for gluconeogenesis from protein would become inevitable for usage of mainly glucose dependent tissues such as brain and nerve cells (Delvin, 1992).

In the diabetic condition, only 5% of an ingested glucose load is converted to fat in an insulin-deficient-diabetic, thus resulting in excess glucose instead of being converted into fatty acid and glycogen for storage is excreted in urine (Hamilton and Bahti, 1987). Also plasma free fatty acid concentrations may rise remarkably due to the mobilization of free fatty acids from adipose tissue by lipolysis of triglycerides. After the glucose level of the blood has been reduced to the physiologically

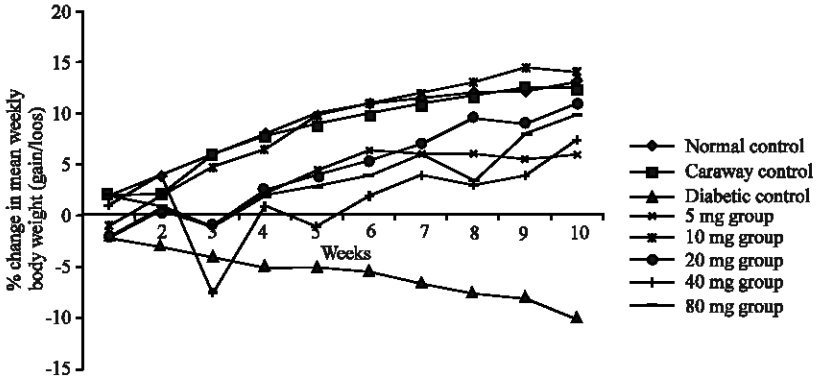

Fig. 1: Percentage changes in the mean weekly body weights of rats in the various animal groups

allowable limit of 70% of the normal fasting level of about 90 mg/100 mL blood, a massive mobilization of storage fat occurs with a subsequent flooding of fatty acids into the liver and kidney (Forster, 1987). The hypoglycaemic effect of the caraway oil at a non toxic level brought all these abnormalities to normal, hence the steady and progressive increment in the % mean weekly body weight at 10 mg kg^{-1} wet weight concentration.

The results obtained from this study support the previous findings as regards black caraway oil and alloxan induced diabetes.

The significant/unique findings of this research connotes that diabetes can be managed with black caraway oil using the correct dose of 10 mg kg^{-1} body weight. It equally shows that diabetic condition can be managed appropriately by improving on the body weight.

CONCLUSION

Since a dose of 10 mg kg^{-1} body weight of black caraway oil in comparison with the other treatment doses significantly brought the blood sugar level of the diabetic rats to normal and equally brought about a steady and progressive increase in the % mean weekly body weight of the diabetic rats, this dose can be considered as the optimum dose that can be used in the management of diabetes mellitus.

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