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The Effect of Different Doses of Black Caraway (*Carum carvi* L.) Oil on the Liver Enzymes of Alloxan-Induced Diabetic Rats

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The effect of different doses of Black caraway oil on the Liver enzymes (i.e., alkaline phosphatase, aspartate amino transferase and alanine amino transferase) of alloxan-induced diabetic rats was studied. Forty white male albino rats of the winster strain weighing between 125-215 g were used. They were divided into eight groups. Diabetes was induced in the experimental rats with alloxan (70 mg kg^{-1} body weight). Group 1 rats served as the normal control, group II served as the caraway control whereas group III served as the diabetic control. Groups IV to VIII were the test groups. They were administered various doses of caraway oil ranging from 5, 10, 20, 40 and 80 mg kg^{-1} body weight respectively. The experiment lasted for a period of 10 weeks. The following liver enzymes were assayed: Aspartate Amino Transferase (ASAT), Alanine Amino Transferase (ALAT) and alkaline phosphatase. Histopathology was also done for the liver. The results showed that the levels of the liver marker enzymes were significantly high ($p<0.05$) in the treatment groups administered with black caraway oil at 20, 40 and 80 mg kg^{-1} body weight. This is also evident in the histopathological analysis of the liver. Due to the fact that the liver marker enzymes were not significantly elevated at 10 mg kg^{-1} body weight and also that the histopathology of the liver did not show any sign of tissue damage at that concentration, the black caraway oil is said to be safe at 10 mg kg^{-1} body weight.

Key words: Black caraway oil, alloxan, diabetes, serum enzymes, albino rats

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INTRODUCTION

Black caraway oil is reported to have hypoglycaemic and hypolipidaemic properties which makes it potent in the management of diabetes mellitus (Modu *et al*., 1997). The caraway plant is known scientifically as *Carum carvi* L. Its other names include bakin algarif (Hausa) and kamum sulum (Kanuri). The plant is indigenous to Europe and Western Asia and is known to have been cultivated since prehistoric time (Kochlar, 1981). The characteristic agreeable aroma and sweet but slightly sharp taste is due to the presence of caraway oil (3-8%) of which carvone is the chief Ketonic constituent (50-60%). The essential oil content of Dutch caraway is relatively high (Pruthi, 1976). The young leaves of the caraway is an important condiment and medicinal agent. It is official in the Indian Pharmacopoeia (1955) and the volatile oil prepared from it is a valuable ingredient of gripe water and other carminative preparation. The volatile oil extracted from the plant has been shown to decrease the arterial blood pressure and heart rate in a dose-dependent manner (El-Tahir *et al*., 1994).

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 and Attia, 1993).

Some work had been done using medical herbs and oil from them in treating diabetes mellitus. The effect s of these herbs and their oils on the levels of various enzymes in the serum and tissue of diabetic rats were studied. In a work done by Ohaeri (2001), it was observed that treatment of diabetic rats with garlic oil significantly decreased the red cell phosphatase ($p<0.01$), serum acid and alkaline phosphatase ($p<0.001$) when compared to diabetic control rats. Serum alanine and aspartate transferases were significantly ($p<0.001$) decreased as well as serum amylase ($p<0.002$) in garlic oil treated diabetic rats as compared with diabetic control rats. In another work done by Shanmugasundaram *et al*. (1983), it was observed that the administration of the dried leaf powder of Gymnema sylvestre controlled phosphorylase levels, gluconeogenic enzymes and sorbitol dehydrogenase in alloxan induced diabetic rabbits. Pathological changes initiated in the liver during the hyperglycemic phase were reversed by controlling hyperglycmia by *G. sylvestre*. In this part of the country, no detailed study had been carried out on the effect of Black caraway oil on the liver enzymes of alloxan induced diabetic rats, execpt this study.

MATERIALS AND METHODS

Forty white male albino rats of the winster strain weighing between 125-215 g were used. The rats were 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 III to VIII rats by injecting them with 70 mg kg^{-1} body weight alloxan administered through the tail after fasting the animals for 24 h (Ajabnoor and Tilmisany, 1988). Twenty four hours after the administration of the alloxan, diabetes was confirmed by 2 h postprandial blood glucose test.

This study was conducted between June and December 2004 at the Biochemistry Department of University of Maiduguri, Nigeria.

Safe dose determination

Treatment regime: Five milligram 10, 20, 40 and 80 mg kg^{-1} body weight of black caraway oil were administered gastrointestinally by intubation to groups IV to VIII rats respectively. Group III rats served as the diabetic control. group II rats which were non-diabetic were given 10 mg kg^{-1} body weight of black caraway oil (caraway control) and group 1 served as the normal control. Treatment continued for 10 weeks. The rats were sacrificed twenty four hours after the last treatment by decapitation.

Collection and treatment of blood and tissues: After the rats were sacrificed by decapitation, the blood was collected in a clean dry centrifuge tube and was allowed to stand for an hour to clot. These samples were centrifuged at room temperature for 10 min and the clear serum samples were then used for the estimation of the liver marker enzymes Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT) and alkaline phosphatase. Blood glucose was estimated from blood obtained from the tail of the rats prior to decapitation. The blood was collected in test tubes prepared with fluoride oxalate to inhibit glycolysis and to prevent coagulation. The rats' liver were collected for histopathological studies.

The method of Reitman and Frankel (1957) was used for the estimation of aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase. For blood sugar estimation, the method of Trinder (1969) was used andthe method of Carleton's histopathological technique by Drury and Wallington (1980) was used for the histopathological studies of the liver.

RESULTS

A general increase was observed in the levels of blood glucose and liver marker enzymes i.e., aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase in the diabetic control rats (Table 1). This increase is statistically significant ($p < 0.01$) compared to the normal control, normal rats fed with caraway oil and the various groups of diabetic rats treated with black caraway oil.

This increase which is as a result of the destruction of the beta cells of the pancreas by Alloxan was brought to near normal in the diabetic rats treated with various concentrations of black caraway oil. Five and ten milligram wet weight concentrations of black caraway oil significantly ($p<0.01$) reduced the levels of blood glucose and liver marker enzymes in the diabetic treatment groups without toxicity to the liver. The 20, 40 and 80 mg wet weight concentrations of the oil could not reduce the levels of the above biochemical parameters in the diabetic treated rats, rather they elevated them. This elevation might be attributed to toxicity of the black caraway oil at higher concentrations. This can also be supported by the results of histopathological studies on the liver tissues of the various groups as shown below.

Results of the histopathological analysis of the liver tissue at the end of 10 weeks

Group I: Normal control
Vacuolar change in liver (Fig. 1)

Group II: Caraway control
Slight fatty change in liver (Fig. 2)

Group III: Diabetic control
The liver (Fig. 3) showed fatty degeneration of the hepatocytes as well as coagulative necrosis.

Group IV: Five milligram wet weight caraway concentration As in group III above

Group V: Ten milligram wet weight caraway concentration Slight fatty change observed in the liver (Fig. 4)

Fig. 1: Liver of rat (Group I i.e., normal control) showing slight vacuolar change (a) (x100)

Fig. 2: Liver of rat (Group II i.e., caraway control) showing slight vacuolar change © (x100)

Fig. 3: Liver of rat (Group III i.e., diabetic control) showing fatty degeneration of the hepatocytes (f) (x100)

Table 1: Biochemical parameters of the normal and diabetic rats treated and untreated with black caraway oil

	Group I normal control	Group II Caraway control	Group III Diabetic control	Group IV 5 mg caraway Rx Group	Group V 10 mg caraway Rx Group	Group VI 20 mg caraway Rx Group	Group VII 40 mg caraway Rx Group	Group VIII 80 mag caraway group
Fasting blood glucose (mmol L^{-1})	5.40 ± 0.57^{d}	4.50 ± 0.58^{d}	14.52 ± 2.08^{a}	8.44 ± 1.15^{b}	7.08 ± 1.15^{bc}	7.90 ± 0.80^{b}	7.83 ± 0.73^{b}	7.30 ± 1.51^{bc}
Alkaline phosphatase) (IU L^{-1})	102.00 ± 0.00^{c}	103.60 ± 5.73^{c}	120.00 ± 2.45^{d}	104.40 ± 3.46^{c}	102.00 ± 3.46^{c}	298.00 ± 19.29^{b}	321.33 ± 38.02^{b}	451.33 ± 65.19^{a}
AST (IU L^{-1})	43.50 ± 3.54^{d}	43.20 ± 1.92^{d}	54.40 ± 2.61^{e}	44.20 ± 2.86^{d}	22.20 ± 2.77^{d}	72.00 ± 4.00^{c}	134.67 ± 17.01^{b}	177.33 ± 1.15^{a}
ALT (IU L^{-1})	22.00 ± 1.40^{d}	22.20 ± 1.30^{d}	32.60 ± 0.89^{e}	22.20 ± 1.30^{d}	22.20 ± 0.84^{d}	48.67 ± 3.06^{c}	73.33 ± 5.03^{b}	126.33 ± 5.51^{a}

-Values are Mean±Standard deviation (n = 5), Values with different superscripts horizontally are statistically different at ($p<0.01$), Rx means treatment

Fig. 4: Liver of rat (Group V i.e., 10 mg Caraway treatment group) showing slight fatty change (I) (x50)

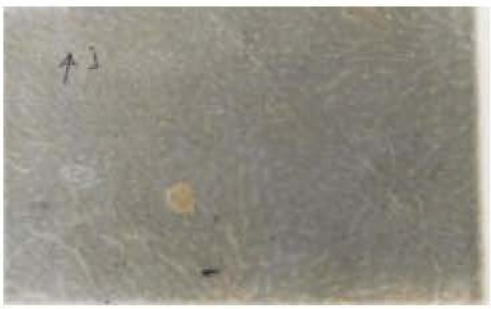

Fig. 5: Liver of rat (Group VIII i.e., 80 mg Caraway treatment group) showing coagulative necrosis (j) (x100)

Group VI: Twenty milligram wet weight caraway concentration Coagulative necrosis of the liver observed

Group VII: Forty milligram wet weight caraway concentration As in VI above

Group VIII: Eighty milligram wet weight caraway concentration There was marked fatty change and coagulative necrosis of the liver (Fig. 5)

DISCUSSION

The elevation in the serum enzymes levels could be explained by the fact that the activity of the serum transaminase enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may be elevated as a consequence of hepatocellular injury and serum alkaline phosphatase may be increased from cholestasis (Rosalki, 1984). Changes in these serum enzymes resulting from alcoholism are most conveniently considered in relation to the stage of the hepatic disorder. In steosis (fatty liver), hepatocellular injury resulting from this may give rise to mild elevation of serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT). On average, the incidence of elevation of these serum enzymes approximates to 20 and 40%, respectively. Both transaminase generally remain below four times the upper reference limit, with aspartate transaminase levels averaging twice the upper reference limit and characteristically higher than alanine aminotransferase (Latner, 1975).

From histopathological studies on the liver of the treatment groups, the toxicity of the black caraway oil increases beyond the dose of 10 mg kg^{-1} body weight. This is in agreement with the study carried out by Modu *et al*. (2001).

CONCLUSIONS AND RECOMMENDATIONS

Since 10 mg concentration of the black caraway oil significantly reduced the level of blood glucose more than the 5, 20, 40 and 80 mg wet weight concentrations of the caraway oil and since the caraway oil is not toxic at the 10 mg wet weight concentration, it can be said that the 10 mg wet weight concentration of the black caraway oil is the safe dose that can be used to manage diabetes mellitus.

A long term effect of 10 mg wet weight concentration of the caraway oil on the experimental rats should also be carried out to be certain that there are no negative effects resulting from long term usage of this oil at 10 mg wet weight concentration.

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