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Full Length Research Paper

Effect of 3-hydroxymethyl xylitol on hepatic and renal functional markers and protein levels in streptozotocin-diabetic rats

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Oral administration of 3-hydroxymethyl xylitol at 40 mg/kg body weight to diabetic rats for 45 days resulted in a significant reduction in blood glucose and significant increase in plasma insulin levels. In addition, the diabetic rats had decreased levels of plasma total protein, albumin, globulin and albumin/globulin ratio as compared to control rats. After treatment with 3-hydroxymethyl xylitol and glibenclamide total protein, albumin, globulin and albumin/globulin ratio were brought back to near normal. The activities of hepatic and renal markers were significantly elevated in diabetic rats as compared to control rats. Treatment with 3-hydroxymethyl xylitol and glibenclamide reversed these parameters to near normal levels. In diabetic rats, the decreased levels of urea, uric acid and creatinine with increased levels of albumin and urine volume was observed, and treatment with 3-hydroxymethyl xylitol and glibenclamide reversed these parameters to near normal. These results indicate that 3-hydroxymethyl xylitol, a compound isolated from *Casearia esculenta,* has beneficial effect on hepatic and renal functional markers.

Key words: *Casearia esculenta,* 3-hydroxymethyl xylitol, glibenclamide, diabetes, liver, kidney, functional markers.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from the defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, espe-cially the eyes, kidneys, nerves, heart, and blood vessels (American Diabetes Association, 2008). The liver and kidney play a major role in the pathogenesis of type 2 diabetes. Nephrotoxicity is one of the major side effects of drug therapy in clinical practice, frequently leading to acute renal failure. Many physiological mechanisms have been implicated in streptozotocin-induced renal injury in diabetes (Babu and Srinivasan, 1998). In diabetes mel-litus, a variety of proteins is subjected to non-enzymatic glycation and is thought to contribute to the long- term complication of the disease (Vlassara et al., 1981). Renewed attention to alternative medicines and natural therapies has stimulated new wave of research interest in traditional practices, and there is a need to look for more efficacious agents with lesser side effects. Recently there is a growing interest in herbal remedies due to the side effects associated with the available oral hypoglycemic agents for the treatment of diabetes mellitus (Kim et al., 2006).

Casearia esculenta Roxb. (Flacourtiaceae) is one such plant in Indian traditional medicine has a popular remedy for the treatment of diabetes (Yoganarasimhan, 2000). Preliminary research revealed a significant blood glucose lowering effect (Prakasam et al., 2002) and antihyperlipidemic activity (Prakasam et al. 2003) after oral administration of *C. esculenta* root extract in normal and streptozotocin-diabetic rats. The active compound, 3-hydroxy-

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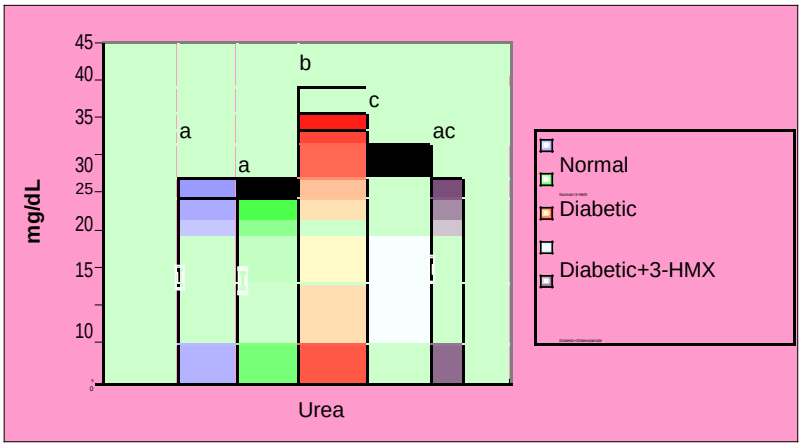
Table 1. Effect of 3-HMX on glucose, insulin, total protein, albumin, globulin and A/G ratio in the plasma of normal and STZ- diabetic rats.

Name of the group	Plasma					
	Fasting Glucose (mg/dl)	Insulin (μU/ml)	Total protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)	A/G ratio
Normal	83.15 ± 6.33^{a}	17.31 ± 0.83^{a}	7.23 ± 0.55^{a}	3.46 ± 0.26^{a}	3.77 ± 0.28^{a}	0.91 ± 0.06^{a}
Normal + 3-HMX (40 mg/kg b.wt.)	69.83 ± 6.45^{b}	18.23 ± 0.81^{b}	7.47 ± 0.56^{a}	3.83 ± 0.29^{b}	3.64 ± 0.27^{ab}	1.05 ± 0.07^{b}
Diabetic control	292.45 ± 4.85^{c}	5.88 ± 0.44^{c}	4.14 ± 0.31^{b}	1.81 ± 0.13^{c}	2.33 ± 0.17^{c}	0.71 ± 0.05^{c}
Diabetic + 3-HMX (40 mg/kg b.wt.)	122.21 ± 6.05^{d}	16.17 ± 0.48^{d}	6.12 ± 0.46^{c}	2.92 ± 0.21^{d}	3.20 ± 0.24^{d}	0.82 ± 0.06^{d}
Diabetic + glibenclamide (600 μg/kg b.wt.)	117.39 ± 5.94^{d}	16.49 ± 0.64^{d}	6.58 ± 0.50^{c}	3.15 ± 0.23^{d}	3.43 ± 0.26^{bd}	0.85 ± 0.06^{ad}

Values are means ± S.D for six rats.
Values not sharing a common superscript differ significantly at $P< 0.05$ (DMRT).

Figure 3. Effect of 3-HMX on urea in the plasma of normal and STZ-diabetic rats.



Values are means ± S.D for six rats.
Values not sharing a common superscript differ significantly at $P< 0.05$ (DMRT).

timated (by using commercially available kits), by the method of Reitman and Frankel, (1957). The activities of serum alkaline phosphatase (ALP) and -glutamyl transferase (-GT) were estimated by the methods of Kind and King, (1954) and Rosalki and Rau, (1972), respectively. Total protein and albumin in the serum were estimated by Biuret method (Reinhold, 1953). Urea in the plasma and urine was estimated by using the diagnostic kit based on the method of Fawcett and Scott, (1960). Uric acid in the plasma and urine was estimated by using the diagnostic kit based on the enzymic method described by Caraway, (1955). Creatinine in the plasma and urine was estimated using the diagnostic kit based on the method of Tietz, (1987) using Jaffe's (1886) colour reaction.

Data were analyzed by one-way analysis of variance followed by Duncan's Multiple Range Test (DMRT) using SPSS version 10 (SPSS, Chicago, IL). The limit of statistical significance was set at $P<0.05$.

RESULTS

The activities of serum liver enzymes in normal and diabetic rats are shown in Figure 1. Increased activities of AST, ALT, ALP and GGT were observed in diabetic's rats. Oral administration of 3-HMX and glibenclamide reversed these parameters towards normalcy.

The body weight changes in normal and diabetic rats are shown in Figure 2 and the levels of glucose, insulin, total proteins, albumin, globulins and albumin/globulin ratio in the plasma of normal and diabetic rats are presented in the Table 1. The diabetic rats had decreased the body weight, increased glucose and decreased levels of plasma insulin, total proteins, albumin, globulins and albumin/globulin ratio when compared with normal rats. After treatment with 3-HMX or glibenclamide showed reversal of these parameters towards normalcy.

The urea, uric acid and creatinine in the plasma of normal and diabetic rats are shown in Figures 3 and 4 respectively. In our study, the levels of urea, uric acid and creatinine elevated markedly in the plasma of diabetic rat