Evaluation of the Hypoglycemic Effect of Plant Proteinase Inhibitors in Rat Diabetes

Brito, MV; Cruz, JWMC; Salu, BR; Oliveira, C; Nunes, NNS; Diniz, PMM; Sampaio, MU; Sannomiya, P; Maffei, FHA; and Oliva, MLV

1Departamento de Bioquímica, Universidade Federal de São Paulo, São Paulo; Brazil; 2Departamento de Cirurgia e Ortopedia, Faculdade de Medicina de Botucatu, Botucatu; Brazil; 3Unidade Cirúrgica de Pesquisa, Universidade de São Paulo, São Paulo, Brazil

Chronic hyperglycemia is a major initiator of diabetic microvascular complications (retinopathy, neuropathy, nephropathy, thrombosis), which are targeted for research for therapeutic options. Plant species of the genus Bauhinia have been used popularly against diabetes without a consistent scientific basis. The objective of this work is to compare the hypoglycemic activity of Bauhinia bauhinioide kallikrein inhibitor (BbKI), a serine peptidase plant Kunitz-type inhibitor to the effect polyspecific inhibitor, EcTI isolated from E. contortisiliquum, that inhibits the digestion enzymes trypsin and chymotrypsin in addition to plasma kallikrein and plasmin which are involved in the intrinsic pathway of blood clotting and fibrinolysis, respectively. The diabetic states were induced intravenously with Alloxan (40 mg/kg) in male Wistar rats (280-320g). After ten days, blood glucose levels were measured, and those animals with glucose levels 250-350 mg/dL were considered diabetic. Seven experimental groups were studied, a non-diabetic and one diabetic, both treated with subcutaneous BbKI or EcTI (0.1 mM/kg), and a diabetic group treated with insulin (6.6 UI/kg). The blood glucose levels were measured at time intervals up to 24 hours. The results showed that BbKI reduced 64% of blood glucose levels in diabetic group only and its effect was prolonged in comparison to that of insulin. No significant decrease on glucose level was observed in the EcTI treated group, indicating that some specific feature in BbKI structure as well its function or enzyme inhibition may be considered for the studies of diabetes.

Supported by: CAPES, FAPESP, FADA/FAP, CNPq
Key Words diabetes; hypoglycemia; insulin; Kunitz inhibitor; proteinase inhibitor