Abstract

Diabetes mellitus is one of the common and very prevalent diseases affecting the citizens of both developed and developing countries. Type 2 diabetes accounts for nearly 80 to 90% of the cases reported. Prominent side-effects of existing drugs are the main reason for an increasing number of people seeking alternative therapies that may have less severe or no side-effects, hence the demand has arisen for using a more benign drug. Natural products have played an important role throughout the world in treating and preventing human diseases. In parts of the world where the population has restricted access to the healthcare system, the use of plants for the treatment of diabetes is widespread. Scientifically, very little is known about the mechanism of action of these traditionally used antidiabetic plants, thus preventing them from being used in standard diabetes care. Consequently, it is necessary to perform toxicological investigation of all plants empirically used in order to avoid the risk of the side effects related to phytotherapy. Recently, more research is being focused on elucidating the action of these plants and their active constituents.

The study aimed at isolating and characterizing antidiabetic principle from *Cucumis prophetarum* L. It is found from literature that, the plant has been explored for anticancer and hepatoprotective effect. However, no studies on antidiabetic and antioxidant activities were previously reported. Hence, in the present study, efforts were made to evaluate antidiabetic activity of active compound and its possible mechanism of action in type 2 diabetic rats from aqueous extract of this fruit.

Aqueous crude extract was fractionated into four different fractions, which were tested for *in vitro* antidiabetic and antioxidant activity. Among these four fractions, fraction 1 showed maximum activity and was characterized using different analytical methods viz., HPLC-DAD, LCMS/MS, 1D-NMR, 2D-NMR and FT-IR. The elucidated structure was found to be a new compound and it was named as N-Trisaccharide. This active compound was further tested for *in vivo* antidiabetic activity in type 2 diabetic rats.

Type 2 diabetes was induced in wistar albino rats using streptozotocin and nicotinamide. The long-term effect of N-Trisaccharide was tested on different
biochemical parameters such as plasma insulin, glycogen and serum lipid levels. Further, in liver and kidney tissues of normal and diabetic rats, the activities of carbohydrate metabolism enzymes *viz.*, hexokinase, glucose-6-phosphatase, fructose-1,6-bisphosphatase, glucose-6-phosphate dehydrogenase, glycogen synthase and glycogen phosphorylase were measured. Enzymatic and non-enzymatic antioxidants such as SOD, CAT, GPx and Vit E, Vit C, GSH were measured respectively. From the results obtained, it was found that N-Trisaccharide possessed significant antidiabetic and antioxidant activities in diabetic rats when compared to standard antidiabetic drug glibenclamide.

Toxicity evaluation studies were carried out in liver and kidney of diabetic rats. Liver damage was assessed by determining DNA damage, hepatic markers *viz.*, SGOT, SGPT and ALP were estimated. Renal dysfunction markers *viz.*, urea and creatinine were measured. Histopathology of pancreas, liver and kidney revealed the non-toxic effect of N-Trisaccharide when compared to standard drug glibenclamide and showed the restoration of normal morphology of islet cells in the pancreas along with improvement in the morphology of liver and kidney in diabetic treated rats.

Present investigation encompasses successful attempts in proving the antidiabetic effect of N-Trisaccharide in type 2 diabetic rats. This active molecule could be used as a template for design and development of new antidiabetic drugs with less or no side effects.

* * * * *