

Russelioside B from *Caralluma quadrangula* improved hepatic glucose metabolism in diabetic rats

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Abstract

Background: Diabetes mellitus (DM) has emerged as a global epidemic, which is predicted to worsen in the coming decades, particularly in developing countries. An alternative strategy to treat diabetes is the use of various natural agents possessing hypoglycemic effect.

Ethnopharmacological relevance: *Caralluma quadrangula* the source of russeliosid B has been used by Bedouins of Saudi communities in cases of thirst and hunger and for the treatment of diabetes, vitiligo, melasma and freckles.

Objective: The present study was aimed to evaluate the improving effect of russelioside B (RB), a major pregnane glycoside isolated from *Caralluma quadrangula* on glucose metabolism in the liver of streptozotocin (STZ)-induced diabetic rats.

Study design: Extraction and isolation of the major pregnae glycoside RB was carried out using chromatographic techniques. RB was identified by comparing its spectral data (¹H- and ¹³CNMR) and melting point with those reported in the literature. The efficacy of RB was investigated on glucose utilization pathways and on hepatic glucose production in STZ-induced diabetic rats, since both of them contribute significantly to plasma glucose level.

Methods: Diabetes was induced by a single intraperitoneal (i.p.) injection of STZ. The rats were assigned in the following groups: **Group 1:** served as normal control group. **Group 2** animals received STZ were served as diabetic group. **Group 3:** this group received daily oral

dose of RB in a dose of 50 mg/kg body weight for 30 days, and served as RB-treated group. At the end of the experimental period, levels of glucose, insulin, and lipid profile including serum total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglyceride (TG) were assayed in the blood serum. On the other hand, a heparinized blood portion was used for the estimation of glycated hemoglobin percentage (HbA1c%). The liver tissue was used to measure glycogen contents, glucose metabolism related enzymes and mRNA expression levels of glucokinase (GK) , Glucose-6-phosphatase (G-6-Pase), glycogen synthase (GS) and glycogen synthase kinase -3 β (GSK-3 β). Body weights of all the animals were recorded prior to the treatment and sacrifice.

Results: The results showed that RB improved the fasting serum glucose level, glycated hemoglobin percent, serum insulin level and lipid profile. The altered activities of the key enzymes of carbohydrate metabolism such as glucokinase, glucose-6-phosphatase, glucose-6-phosphate dehydrogenase, and glycogen phosphorylase in liver of diabetic rats were significantly improved by the administration of RB. Further, RB administration to diabetic rats reverted gene expression of glucokinase, glucose-6-phosphatase, glycogen synthase and glycogen synthase kinase-3 β to near normal levels.

Conclusion: To the best of our knowledge, this is the first mechanistic study of the antidiabetic activity of RB glycoside or related pregnane glycosides in animal model. Since, RB exhibited anti-hyperglycemic and anti-hyperlipidemic potential, which acts by improving insulin secretion and the alterations in the carbohydrate and lipid metabolism. We can conclude that administration of RB isolated from aerial parts of *Caralluma quadrangula* may represent a potentially useful strategy for the management of diabetes. Further clinical investigation in human will be undertaken in future study.

Key words: *Caralluma quadrangula*, Russelioside B, Streptozotocin, Diabetes, Rat, Carbohydrate metabolizing enzymes