Modulation of glucose metabolism-related genes in diabetic rats treated with herbal synthetic anti-diabetic compound (α-HSA): insights from transcriptomic profiling

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Abstract

Background: Eugenia jambolana is a medicinal plant traditionally used for treating diabetes. The bioactive compound FIIc, which is derived from the fruit pulp of E. jambolana, has been identified and purified as α-HSA. Previous studies have demonstrated that administration of α-HSA for 6 weeks improved glycemic index and dyslipidemia in rats with T2D.

Objectives: This study investigated the molecular mechanism underlying the potential therapeutic effects of α-HSA in experimentally induced diabetic rats.

Methods: Male Wistar rats were divided into four groups: diabetic control, diabetic treated with FIIc, diabetic treated with α-HSA, and diabetic treated with glibenclamide. Over a 6-week experimental period, transcriptomic analysis was conducted on liver, skeletal, and pancreatic tissue samples collected from the rats.

Results: The study findings revealed significant upregulation of genes associated with glucose metabolism and insulin signaling in the groups treated with FIIc and α-HSA, compared to the diabetic control group. Moreover, pro-inflammatory genes were downregulated in these treatment groups. These results indicate that α-HSA has the potential to modulate key metabolic pathways, improve glucose homeostasis, enhance insulin sensitivity, and alleviate inflammation.

Conclusions: This study provides compelling scientific evidence supporting the potential of α-HSA as a therapeutic agent for diabetes treatment. The observed upregulation of genes related to glucose metabolism and insulin signaling, along with the downregulation of pro-inflammatory genes, aligns with the pharmacological activity of α-HSA in controlling glucose homeostasis and improving insulin sensitivity. These findings suggest that α-HSA holds promise as a novel therapeutic approach for managing diabetes and its associated complications.

Keywords: Eugenia jambolana; diabetes; glucose metabolism; insulin sensitivity; transcriptomic analysis; α-HSA.

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Research Article

Herbal Anti-Hyperglycemic Compound Increases Expression of Glucose Transporter Molecules in Diabetic Rats

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ABSTRACT

Background: In previous studies, Sharma et al. has already isolated an anti-hyperglycemic compound from the fruit pulp of *Eugenia jambolana* using HPLC and other chromatographic techniques. However, the effect of anti-hyperglycemic compound (FIIc) on the expression of Glucose transporters and Kv 1.3 potassium channel in Streptozotocin-Nicotinamide induced diabetic rats has not been studied so far.

Objective: To study the effect of HPLC purified herbal anti-hyperglycemic compound (FIIc) on the expression of GLUT-4, GLUT-8 and Kv 1.3 potassium channel in Streptozotocin-Nicotinamide induced diabetic rats.

Methods: 24 Male Wistar rats were taken and diabetes was induced in group B, C and D rats (n=6 each) by injecting Streptozotocin at a dose of 45 mg/kg of body weight 15 minutes after the administration of Nicotinamide at a dose of 230 mg/kg of body weight, intraperitoneally to overnight fasted rats. Active compound (FIIc) was orally administered to group C and Pioglitazone to group D at a dose of 20 mg/kg of body weight for 6 weeks respectively. Serum was separated for the estimation of Adiponectin and TNF alpha at week 0 and week 6 of the study. Real time mRNA expression of GLUT-4, GLUT-8 and Kv 1.3 potassium channel was measured and compared between healthy and diabetic control rats. Expression of GLUT-4, GLUT-8 and Kv 1.3 potassium channel was also measured at protein level through Immunohistochemistry and compared between healthy and diabetic controls.

Results: After treatment with FIIc for 6 weeks there was a 1.28 folds increase in GLUT-4 mRNA expression in skeletal muscles and 2.67 folds increase in GLUT-8 mRNA expression in liver tissues of group C rats as compared to group B rats. However, Kv 1.3 potassium channel mRNA expression was found to be at par among the four study groups. TNF alpha levels were found to be significantly decreased in group C rats as compared to group B. A slight increase in serum Adiponectin level was observed in group C as compared to group B, which was found to be statistically insignificant.

Conclusion: FIIc treatment for 6 weeks significantly increases the expression of GLUT-4, GLUT-8 mRNA expression in liver and skeletal muscles leading to increased peripheral insulin sensitivity.

Keywords: *Eugenia Jambolana*; FIIc; Diabetes; GLUT 4; GLUT 8; Kv 1.3 Potassium Channel; Pioglitazone; Wistar rats; HPLC

INTRODUCTION

Mammalian cells utilize glucose for the generation of energy in the form of ATP. With the help of glucose transporter proteins, the blood glucose is taken up by the mammalian cells which are encoded by the SLC2 genes [1,2].

GLUT-4 is the primary glucose transporter responsible for insulin stimulated glucose uptake into muscle and adipose tissues. Studies have reported that during diabetes, the insulin-stimulated glucose uptake by GLUT-4 is largely hampered in muscle and adipose tissue leading to the development of insulin resistance. Studies have also reported that over expression of GLUT-4 in the adipose tissue of GLUT-4 knockout mice ameliorate insulin resistance, diabetes and enhance insulin sensitivity [3-6].

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