Upregulation of insulin secretion and downregulation of pro-inflammatory cytokines, oxidative stress and hyperglycemia in STZ-nicotinamide-induced type 2 diabetic rats by Pseudozaria monticola bark extract

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ABSTRACT

The current study aimed to ascertain the antidiabetic potential of Pseudozaria monticola bark methanolic extract (PMM) using in vitro mechanistic study models. In particular, the study determined the effect of PMM on cellular viability, 2-NDBG glucose uptake, insulin secretion, and NF-κB translocation in mouse pancreatic islet cells (MIN-1). Furthermore, in vitro acute toxicity and antidiabetic studies were performed using streptozotocin (STZ)-induced type 1 and STZ-nicotinamide-induced type 2 diabetic rat models to evaluate various biochemical parameters and markers of oxidative stress and pro-inflammatory cytokines. Five isoquinoline alkaloids and three phenolic compounds were tentatively identified in the PMM by LC/MS Triple TOF. The study results showed that PMM is non-toxic to MIN-1 cells and significantly increased the glucose uptake and insulin secretion without affecting the translocation of NF-κB. Moreover, the non-toxic effects of PMM were confirmed through an in vivo acute toxicity study, which revealed that the serum insulin and C-peptide levels were significantly upregulated in type 2 diabetic rats and that no significant changes were observed in type 1 diabetic rats. Similarly, PMM was found to downregulate the levels of oxidative stress and pro-inflammatory cytokines in type 2 diabetic rats by alleviating hyperglycemia. Therefore, we conclude that PMM may be developed as an antidiabetic agent for the treatment of type 2 diabetes-associated conditions.

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder in the endocrine system characterised by abnormally high levels of glucose in the blood (Arya et al., 2012a). DM is categorised into type 1 and type 2 diabetes. Type 1 diabetes mellitus (T1DM) is caused by impaired insulin secretion from pancreatic β-cells, whereas type 2 diabetes mellitus (T2DM) is characterised by carbohydrate, lipid, and protein disorders and defects in insulin signalling involving insulin resistance. T2DM’s prevalence is closely related to obesity due to the practice of an unhealthy sedentary lifestyle (Crawford et al., 2010). It was purported by the International Diabetes Federation (IDF) that the number of diabetic cases will increase from 194 million in 2003 to 333 million by the year 2025 (Zimmet et al., 2003). Hyperglycaemia, a characteristic of diabetes, has been shown to increase the production of reactive oxygen species (ROS) and promote oxidative stress resulting in the reduction of antioxidant levels. Previous studies have also demonstrated the relationship between oxidative stress and inflammatory cytokines in diabetic nephropathy (Elmarakby and Sullivan, 2012).

A variety of plants that were traditionally used in the treatment and management of diabetes mellitus in folk medicine are known to demonstrate antidiabetic properties (Jung et al., 2006a; Paydar et al., 2013a,b). The active chemical constituents isolated from these plants that are responsible for these hypoglycaemic properties include glycosides, flavonoids, phenolics, steroids, alkaloids, and terpenoids (Sharma et al., 2010; Chung et al., 2011).