

***CENTAURIUM ERYTHRAEA* EXTRACT MEDIATES PRO-SURVIVAL PATHWAYS AND INSULIN EXPRESSION IN STZ-TREATED BETA-CELLS**

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Diabetes is characterized by hyperglycaemia resulting from a deficiency in insulin secretion and/or action leading to severe diabetic complications. Despite numerous efforts, recovery and maintenance of functional beta-cells is still an unresolved task in diabetes therapy. Considering anti-diabetic properties of medicinal herb *Centaurium erythraea* Rafn (CE), this study aimed to analyze protective effects of the CE extract on Rin-5F beta-cell line exposed to diabetogenic agent streptozotocin (STZ). Cytoprotective concentration of CE extract (0.25 mg/mL) and IC₅₀ dose of STZ (12mM) were determined using cell viability assay (MTT). The level of insulin mRNA and the concentration of insulin released from beta-cells in a culture medium were analyzed by RT-qPCR and ELISA, respectively. Activity of Akt, ERK and p38 kinases, as well as nuclear levels of islet-enriched Pdx1 and MafA proteins were assessed by Western blot analysis. In comparison to STZ-treated cells, CE extract/STZ co-treatment increased viability of Rin-5F cells for 12%. STZ-treated beta-cells displayed reduced mRNA level of insulin to 63% and reduced insulin secretion to 76% in comparison to controls, while application of CE extract improved insulin mRNA level to 77% and insulin secretion to 90% of the control level. Improved viability and functionality of beta-cells could be ascribed to a CE extract-mediated modulation of the activities of pro-survival Akt, ERK and p38 kinases and Pdx-1 and MafA factors involved in regulation of beta-cell proliferation and insulin expression/secretion. The results of this study suggest that CE extract promotes proliferative and pro-survival pathways in beta-cells and improves their functional properties.

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