Fernenodiol [Fern-9(11)-eno-2α,3β-diol] triterpene treatment enhances insulinotropic effects in hyperglycemic rats

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Introduction and objectives: Once antidiabetic agents from natural sources have low toxicity and reduced side effects when compared to the current oral hypoglycemic drugs [1, 2], natural compounds that normalize glycemia of diabetic/insulin resistant individuals are extremely important in pharmacological use. This investigation aimed to study the anti-hyperglycemic effect of fernenodiol [fern-9(11)-eno-2α,3β-diol] triterpene and its mechanism of action on glucose homeostasis. Material and methods: Wistar rats were high glucose-induced hyperglycemia following treatment with fernenodiol (0.1, 1 and 10 mg/Kg). Initially, serum levels of glucose, insulin and LDH, and total hepatic glycogen content were measured. Next, isolated pancreatic islets were used for in vitro glucose uptake and calcium influx assays. The mechanism of action of fernenodiol were evaluated by the following substances: blocker (glibenclamide) and activator (diazoxide) of ATP-sensitive potassium channel (K\textsubscript{ATP}), blocker (nifedipine) of L-type voltage-dependent calcium channel (Ca\textsubscript{v}), intracellular calcium chelator (BAPTA-AM), and PKA (H-89) and PKC (stearoylcarnitine) inhibitors. Results and conclusion: In all three doses, fernenodiol caused an anti-hyperglycemic effect, such as decreased serum glucose level (up to 26%), enhanced glucose-induced insulin secretion (up to 18%) and increased hepatic glycogen accumulation (up to 4-fold). Additionally, a positive effect on glucose uptake (3.5-fold) and calcium influx (2.4-fold) was stimulated by this compound at respective concentrations of 100 pM and 1 nM in pancreatic islet. The mechanism of action of fernenodiol involves K\textsubscript{ATP} and L-type Ca\textsubscript{v} contribution. Despite its action be independent of PKA and PKC activity, the intracellular calcium mobilized by this triterpene suggests its action in a second phase-like insulin secretion. To our knowledge, this is the first time that the biological activity of this compound is explored and characterized. In summary, the low toxicity and the strong insulinotropic effects implicate fernenodiol as a potent pharmacological agent for additional studies focusing on diabetic/insulin resistance therapy.

Word Keys: triterpen, glucose homeostasis, insulin secretion

References: