Effect of liquiritigenin on apoptotic beta-cell death by palmitate-induced lipotoxicity in INS-1 cells

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Abstract

Objective: Activation of estrogen receptor signaling plays an important role to preserve functional beta-cell mass in treatment of diabetes. Liquiritigenin (LQ), a flavonoid isolated from *Glycyrrhiza uralensis*, is an estrogenic compound which acts as an agonist for the estrogen receptor β. In this study, we investigated protective effect of LQ on palmitate (PA)-induced apoptosis in INS-1 cells.

Methods: To examine effect of LQ on beta cells, glucose stimulated insulin secretion (GSIS) by enzyme immunoassay (EIA) method and cell viability by MTT were measured in rat beta-cell line INS-1 cells. To induce lipotoxicity, PA (400 μM) was treated for 24 h and amount of apoptotic cells were analyzed using a flow cytometer with annexin-V staining. Expression level of apoptotic proteins and endoplasmic reticulum (ER) stress markers were analyzed by western blot analysis after LQ treatment. Tunicamycin and thapsigargin were used to ER stress inducer and AKT inhibitor (AKTi-1/2) was used to inhibit LQ-induced AKT phosphorylation at ser 473.

Results: Exposure of INS-1 cells to 5 μM of LQ significantly increased GSIS as well as cell viability. PA treatment increased annexin-V stained cells and apoptotic proteins such as cleaved caspase-3, cleaved poly (ADP-ribose) polymerase and bax, but these increases were significantly inhibited by LQ treatment. LQ treatment inhibited cell death by ER stress inducers and PA induced ER stress marker proteins such as CHOP and phosphorylated forms of PERK and eIF2α was also significantly downregulated in LQ treated cells. LQ phosphorylated AKT at ser 473 via estrogen receptor element dependent pathway and blocking AKT signaling inhibited LQ induced decrease in level of phosphorylated PERK, consequently cell viability was not recovered.

Conclusion: Our data demonstrated that LQ has anti-apoptotic effect against PA induced lipotoxicity and AKT mediated ER stress inhibition was involved in the anti-apoptotic effect of LQ.

Image

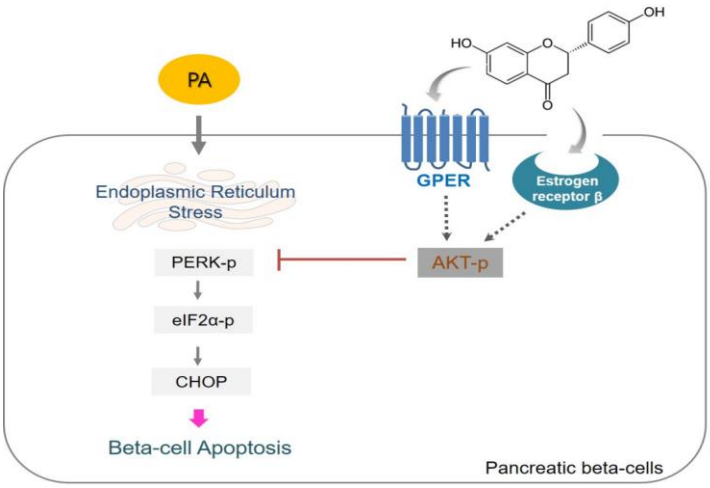

Fig. 1 The proposed molecular mechanisms of the LQ-mediated anti-apoptotic effect in INS-1 cells treated with PA.

Recent Publications

1. Bae GD, Park EY, Baek DJ, Jun HS, Oh YS (2018) Liquiritigenin prevents palmitate-induced beta-cell apoptosis via estrogen receptor-mediated AKT activation. Biomedicine & Pharmacotherapy 101: 348-354
2. Jun HS, Bae GD, Ko YT, Oh YS (2015) Cytotoxicity and Biological Efficacy of Exendin-4-Encapsulated Solid Lipid Nanoparticles in INS-1 Cells. Journal of Nanomaterials 2015: 1-6
3. Oh YS, Seo E, Park K, Jun, HS (2017) Compound 19e, a Novel Glucokinase Activator, Protects against Cytokine-Induced Beta-Cell Apoptosis in INS-1 Cells. Frontiers in Pharmacology 8,169: 1-10
4. Oh YS, Shin S, Li HY, Park EY, Lee SM, Choi CS, Lim Y, Jung HS, Jun HS (2015) Betacellulin ameliorates hyperglycemia in obese diabetic db/db mice. Journal of Molecular Medicine 93: 1235-1245

Biography

Gong Deuk Bae is a PhD course student in Gachon university. His research topic is The effect of natural products on the prevention and treatment of type 2 diabetes focusing on pancreatic beta-cells.

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Notes/Comment