Abstract

Data obtained from observational studies have shown that use of statins is associated with the increase of risk type 2 diabetes. It has been reported that lipophilic statins such as atorvastatin can more readily penetrate into β-cells and reach the mitochondria, resulting in mitochondrial dysfunction, oxidative stress, decrease in insulin release. Many studies have shown that natural products can protect mitochondrial dysfunction induced by drug in different tissue. For this purpose, the aim of current study was to explore mitochondrial protection potency of hesperidin as a natural compound against atorvastatin-induced mitochondrial dysfunction in pancreas isolated mitochondria.

materials and methods:

Using mechanical lysis and differential centrifugation, mitochondria were isolated from rat pancreas and directly exposed to the toxic concentration of atorvastatin (500 µM) in the presence of different concentrations of hesperidin (1, 10 and 100 µM) separately. Succinate dehydrogenase (SDH) activity, reactive oxygen species (ROS) production, mitochondrial swelling, mitochondrial membrane potential (MMP), glutathione (GSH) depletion, and malondialdehyde (MDA) production as parameters of mitochondrial toxicity caused by atorvastatin in one hour It was measured.

Results:

Our findings demonstrated that atorvastatin directly induced mitochondrial toxicity at concentration of 500 µM and higher in pancreatic mitochondria. Except MDA, atorvastatin caused significantly reduction in SDH activity, ROS formation, mitochondrial swelling, collapse of MMP and depletion of GSH in rat pancreas isolated mitochondria. While, our data showed that protective compound at low concentrations ameliorated atorvastatin-induced mitochondrial dysfunction with the increase of SDH activity, improvement of MMP collapse, mitochondrial swelling and mitochondrial GSH, and reduction of ROS formation in pancreas isolated mitochondria.

Discussion and conclusion:

We can conclude that hesperidin can directly reverse the toxic of atorvastatin in rat pancreas isolated mitochondria, which may be beneficial for protection against diabetogenic-induced mitochondrial dysfunction in pancreatic β-cells.

Key Words: Statins; Diabetogenic Drug; Antioxidants; Diabetes Prevention; Anti-prediabetic Effects