

Abstract

Introduction

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 vanillic acid as 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 treated with toxic concentrations of atorvastatin (500 μ M) in presence of various concentrations vanillic acid (1, 10 and 100 μ M) separately. Mitochondrial toxicity parameters such as the succinate dehydrogenases (SDH) activity, reactive oxygen species (ROS) formation, mitochondrial swelling, mitochondrial membrane potential (MMP) collapse, depletion of glutathione (GSH) and malondialdehyde (MDA) production were measured during 1 hour in rat pancreas isolated mitochondria.

Results

Our findings demonstrated that atorvastatin directly induced mitochondrial toxicity at concentration of 500 μ M 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 all 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

We can conclude that vanillic acid 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; Vanillic acid; Atorvastatin; Mitochondrial toxicity; Diabetogenic Drug; Antioxidants; Diabetes Prevention; Anti-prediabetic Effects