World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:10, No:08, 2016

Metformin Protects Cardiac Muscle against the Pro-Apoptotic Effects of Hyperglycaemia, Elevated Fatty Acid and Nicotine

Authors : Christopher R. Triggle, Hong Ding, Khaled Machaca, Gnanapragasam Arunachalam

Abstract : The antidiabetic drug, metformin, has been in clinical use for over 50 years and remains the first choice drug for the treatment of type two diabetes. In addition to its effectiveness as an oral anti-hyperglycaemic drug metformin also possesses vasculoprotective effects that are assumed to be secondary to its ability to reduce insulin resistance and control glycated hemoglobin levels; however, recent data from our laboratory indicate that metformin also has direct vasoprotective effects that are mediated, at least in part, via the anti-ageing gene, SIRT1. Diabetes is a major risk factor for the development of cardiovascular disease (CVD) and it is also well established that tobacco use further enhances the risk of CVD; however, it is not known whether treatment with metformin can offset the negative effects of diabetes and tobacco use on cardiac function. The current study was therefore designed to investigate 1: the effects of hyperglycaemia (HG) either alone or in the presence of elevated fatty acids (palmitate) and nicotine on the protein expression levels of the deacetylase sirtuin 1 (the protein product of SIRT1), anti-apoptotic Bcl-2, pro-apoptotic BIM and the pro-apoptotic, tumour suppressor protein, acetylated p53 in cardiomyocytes. 2: the ability of metformin to prevent the detrimental effects of HG, palmitate and nicotine on cardiomyocyte survival. Cell culture protocols were designed using a rat cardiomyocyte cell line, H9c2, either under normal glycaemic (NG) conditions of 5.5mM glucose, or hyperglycaemic conditions (HG) of 25mM glucose with, or without, added palmitate (250μM) or nicotine (1.0mM) for 24h. Immuno-blotting was used to detect the expression of sirtuin 1, Bcl-2, BIM, acetylated (Ac)-p53, p53 with β-actin used as the reference protein. Exposure to HG, palmitate, or nicotine alone significantly reduced expression of sirtuin1, Bcl-2 and raised the expression levels of acetylated p53 and BIM; however, the combination of HG, palmitate and nicotine had a synergistic effect to significantly suppress the expression levels of sirtuin 1 and Bcl-2, but further enhanced the expression of Ac-p53, and BIM. The inclusion of 1000μM, but not 50μM, metformin in the H9c2 cell culture protocol prevented the effects of HG, palmitate and nicotine on the pro-apoptotic pathways. Collectively these data indicate that metformin, in addition to its anti-hyperglycaemic and vasculoprotective properties, also has direct cardioprotective actions that offset the negative effects of hyerglycaemia, elevated free fatty acids and nicotine on cardiac cell survival. These data are of particular significance for the treatment of patients with diabetes who are also smokers as the inclusion of metformin in their therapeutic treatment plan should help reduce cardiac-related morbidity and mortality.

Keywords : apoptosis, cardiac muscle, diabetes, metformin, nicotine
Conference Title : ICPPM 2016 : International Conference on Pharmacology and Pharmaceutical Medicine
Conference Location : Vancouver, Canada
Conference Dates : August 04-05, 2016