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Studies on the cardioprotective actions of myrcetin and kaempferol in ischemia reperfusion induced myocardial infarction in normal and stz induced type-i diabetic rats

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Abstract

Diabetic individuals are at increased risk for cardiovascular morbidity and mortality compared to the general population and portends a worse prognosis. Patients with type 1 diabetes exhibit a risk of cardiovascular mortality up to 10 times higher than non-diabetic subjects. As a result, diabetics are more likely to encounter situations of myocardial ischemia and reperfusion. Flavonoids such as Myricetin and Kaempferol have received much attention in the area of nutritional biology .In spite of tremendous potentiality of Myricetin and Kaempferol to protect the heart during ischemia-reperfusion, only few studies reported the cardioprotective actions of Myricetin and Kaempferol in ischemia reperfusion injury. However, cardioprotective mechanisms of Myricetin and Kaempferol have not been so far explored in ischemia-reperfusion of diabetic hearts. The objective of the present investigation is to evaluate the cardioprotective actions and mechanisms of Myricetin and Kaempferol against ischemia reperfusion injury in both normal and diabetic rats

Key words: Myocardial infarction, ischemia reperfusion, myrcetin, kaempferol, anti-oxidants.

Introduction

Ischemic heart disease (IHD) is the general designation for a group of closely related syndromes resulting from ischemia, an imbalance between the supply and demand of the heart for oxygenated blood. Myocardial ischemia is a disorder of cardiac function caused by insufficient blood flow to the heart muscle. There are various causes of myocardial ischemia. Atherosclerosis in the coronary arteries and coronary thrombosis are the commonest pathological disorders that lead to myocardial ischemia. Angina pectoris and acute myocardial infarction are two clinical manifestations of myocardial ischemia. These and other closely related heart conditions are classified under the category of ischemic (or coronary) heart diseases. Ischemic injury depends upon the length of ischemia (Bolli, 1990). The heart can recover gradually from a short duration of ischemia (reversible ischemia), but if ischemia persists for a longer period of time, the chance for recovery will diminish (irreversible ischemia) (Bolli, 1990).

Myocardial ischemia and Reperfusion injury

Coronary artery bypass grafting (CABG), Percutaneous transluminal coronary angioplasty (PTCA) or thrombolytic therapies are the treatment options for acute myocardial infarction to reestablish the blood flow to the ischemic myocardium. Reperfusion of myocardium, sufficiently early after the onset of ischemia may prevent all necrosis. Reperfusion after a long interval can prevent necrosis of at least some myocytes that would otherwise die with prolonged or permanent ischemia. Myocardial ischemia of limited duration (<20 min) followed by reperfusion is accompanied by functional recovery without morphologic and biochemical evidence of irreversible ischemic injury

(Lucchesi 2001). Paradoxically, reperfusion of cardiac tissue that has been subjected to an extended period of ischemia (> 45 min) results in a phenomenon is known as "reperfusion injury" (Lucchesi, 2001). Reperfusion injury originally defined by Hearse et al.,(1973) as the sudden release of intracellular constituents (majorly creatine kinase and lactate dehydrogenase) from heart tissue upon reoxygenation after a period of hypoxia (Hearse et al.,1973). Today, reperfusion injury is much more broadly defined as cell death induced by reperfusion of myocytes that were still viable before reperfusion (Ambrosio and Chiariello, 1985; Werns et al., 1985).

Materials and Methods

Myricetin dihydrate (3,5,7-Trihydroxy-2-(3,4,5-trihydroxyphenyl)-4-chromenone) was sourced from Sigma Chemical Co. (St. Louis, USA). The beneficial effects of Myricetin include anti-oxidant, anti-inflammatory, cardiovascular protection, anti-cancer activity, anti-ulcer effects, anti-allergic activity and antiviral activity. Kaempferol hydrate (3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one) was sourced from Sigma Chemical Co. (St. Louis, USA). Kaempferol as a strong antioxidant suppresses various free radical-mediated processes such as in vitro lipid peroxidation. In addition to anti oxidant activity, it also possesses anti cancer activity and anti microbial activity. Streptozotocin (Product No's: 046K1206, 076K1479 and Cat No. S0130) purchased from Sigma Chemical Co. (St. Louis, USA) for induction of diabetes.

Animals

Albino Wistar rats (National Institute of Nutrition, Hyderabad, India) of either sex weighing 175 – 275 g were used in the study. Animals were maintained under standard laboratory conditions at 25 ⍰ 20 C, relative humidity 50 ⍰ 15% and normal photoperiod (12 h dark/ 12 h light) and were used for the experiment. Commercial pellet diet (Rayons biotechnologies Pvt Ltd, India) and water were provided ad libitum. The experimental protocol has been approved by the Institutional Animal Ethics Committee and by the Animal Regulatory Body of the Government (Regd. No. P6/VCP/IAEC/2012/4/AE13).
Induction of Diabetes

Diabetes was induced by a single intravenous injection of streptozotocin (STZ) 45 mg/kg of body weight, dissolved in citrate buffer (pH 4.5) into the tail vein of animals anaesthetized with ether. Diabetes was confirmed by estimations made after third day of STZ injection for serum glucose by a semi auto analyzer (Screen Master 3000, USA). Following two weeks of diabetes induction, rats were subjected to surgical procedure. About 20% of mortality was observed in diabetic rats even before being subjected to ischemia-reperfusion injury. Diabetic rats showing more than 350 mg/dl were used for the experiment.

Surgical procedure

Rats were anaesthetized with thiopentone sodium (30 mg/kg, intraperitoneal). The neck was opened with a ventral midline incision and intubated through a tracheotomy and ventilated with room air by a techno positive pressure respirator (Crompton Parkinson Ltd., England). The body temperature was monitored and maintained at 370C throughout the experimental protocol. A left thorocotomy and pericardiotomy were performed, followed by identifying the marginal branch of the left anterior descending coronary artery (LAD). A silk thread (4-0) was passed behind the artery and was occluded by a knot for 30 min. The silk thread was removed after 30 min with the help of two knot releasers to allow reperfusion of the heart for succeeding 4 h. Whereas, the sham control animals were subjected to the entire surgical procedure and thread was passed beneath the coronary artery, but the coronary artery was not ligated.
Equal numbers of both male and female rats were used in this study. There were no significant gender differences in infarct size in control or treated rabbits (Schriefer et al., 2001). Thus male and female values were combined in the present study.

Conclusion

From the Experimental studies, Selected Flavonols like Myricetin and Kaempferol has a potential to exhibit the cardio protective effects in Normal And STZ Induced Type I Diabetic Rats and possesses a significant medicinal value in the prophylactic treatment of MI. We successfully achieve the First objective of the study is to evaluate the cardioprotective actions of Myricetin and Kaempferol against ischemia-reperfusion induced myocardial infarction in normal and STZ induced Type I diabetic rats. And also successfully established the mechanisms like Anti-Oxidant role, Anti- inflammatory role involved in the cardioprotective actions of Myricetin and Kaempferol. The following parameters like serum and tissue malanoldihyde, SOD, Catalase, Myeloperoxidase, Serum interleukin-12 are studied in the present investigation. The search for new mechanism for cardio protective activity is an important issue, as the trend toward using bioflavonoids of high quality, safety and efficacy will continue. Therefore, all efforts have to be targeted to reveal the chemical- pharmacological profiles and fixed combinations and to rationalize their therapeutic application.

Conflict of Intresr

The author deleres no cinflict of Intrest

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