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The protective effect of epicatchin against oxidative stress and nephrotoxicity in rats induced by cyclosporine

Abdulrahman L Al-Malki and Said S Moselhy

Abstract

Cyclosporine A (CyA) is the first-line immunosuppressant used for the management of solid organ transplantation and autoimmune diseases. Reactive oxygen species (ROS) can attack all types of macromolecules including DNA and damage it. Epicatechin (EC) is one of the most potent antioxidants present in the human diet. Particularly high levels of this compound are found in tea, apples, and chocolate. The goal of this study was to evaluate the protective effect of EC against CyA toxicity and its antioxidant activity in transplanted patients to avoid its side effects. Results obtained showed that, CyA exert its toxic effect by increasing the free radicals and ROS that causes lipid peroxidation and cell damage, this is detected by elevation of hydroperoxides and thiobarbituric acid reactive substances, while the activities of antioxidant enzymes include (superoxide dismutase [SOD], catalase [CAT] and glutathione peroxidase [GPx]) were significantly decreased as compared with control rats. The deleterious toxic effects of CyA are, at least in part, due to increased production of free radicals and ROS. Treatment of rats with epicatchin ameliorates the toxicity of CyA by decreasing the lipid peroxidation and enhanced the antioxidants enzyme activities.

Keywords

cyclosporine, epicatchine, oxidative stress

Introduction

Nephrotoxicity is the major reported side-effect of cyclosporin in transplanted patients.[1] Apart from primates, the rat appears to be one of the few laboratory species susceptible to cyclosporin-induced nephropathy and has been proposed as a model of the morphologic and functional changes that occur in the human.[2] A reduced glomerular filtration rate and renal tubular change have been reported following oral administration of cyclosporin at 50 mg/kg/day for 14 days to Sprague–Dawley adult rats.

Cyclosporin-induced arteriolopathy in the kidney has been reported in the spontaneous hypertensive rat but not in any normotensive rat strain. Cyclosporin-induced adverse renal effects in humans are usually rapidly reversible.[3,4]

The rat may be an inappropriate model for cyclosporin-induced nephropathy in the juvenile, due to differences in the chronology of renal development with respect to the human.[5] Nephrogenesis is largely post-natal in the rat but occurs before birth in the human.[6] It is likely, therefore, that the more anatomically advanced kidney of the human infant would be less vulnerable than that of the rat pup to the adverse effects of cyclosporin, particularly if the effects in the rat are induced early in neonatal life. Nephropathy has been reported in the rabbit following in utero exposure to cyclosporin,[7] a species in which nephrogenesis occurs prenatally as in the human.

An imbalance between the formation and removal of reactive oxygen species (ROS) and the development of oxidative stress has been widely purported

Biochemistry Department, Faculty of Science, King Abdualziz University, Jeddah, KSA

Corresponding author:
Said S Moselhy, Biochemistry Department, Faculty of Science, King Abdualziz University, Jeddah, Saudi Arabia
Email: Moselhy6@hotmail.com