1,2-Diazole prevents cisplatin-induced nephrotoxicity in experimental rats

Venugopal Vinod Prabhu, Narayanan Kannan, Chandrasekharan Guruvayoorappan

Department of Biotechnology, Karunya University, Karunya Nagar, Coimbatore - 641 114, Tamil Nadu, India

Correspondence: Chandrasekharan Guruvayoorappan, e-mail: immunologykarunya@gmail.com, gurukanunya@gmail.com

Abstract:
Background: Cisplatin (a platinum-compound) is a anti-neoplastic drug used in the treatment of various cancers but eventually results in severe adverse effects namely nephrotoxicity or renal disorder through generation of reactive oxygen species (ROS). This biochemical measurements and histopathology analysis investigated a possible protective effect of 1,2-diazole with regards to cisplatin-induced nephrotoxicity in experimental animals.

Methods: Animals were divided into four groups of six mice each. Group A: normal control, vehicle (1% w/v) gum acacia in phosphate buffer saline (PBS). Group B: cisplatin group, vehicle + cisplatin (7.5 mg/kg). Group C: 1,2-diazole (10 mg/kg) + cisplatin and Group D: silymarin (50 mg/kg) + cisplatin. Each vehicle/drug treatment was given daily via intraperitoneal (ip) injection for 10 consecutive days starting from day 1. On group B, C and D cisplatin was given in single dose only on day 5 one hour post drug administration. Animals were allowed till 10th day and on day 11 all four groups animals were anesthetized. Blood samples were collected and serum was isolated for biochemical measurements. The rats were then euthanized by cervical dislocation and their kidneys were collected and were preserved for biochemical measurements and histopathology analyses.

Results: Pretreatment with 1,2-diazole prevented nephrotoxicity induced by cisplatin through a protective mechanism that involved reduction of increased oxidative stress by significantly increasing the enzymatic and non enzymatic antioxidant enzymes such as glutathione peroxidase (GPx), glutathione (GSH) and diminishing the lipid peroxidation (LPO). The pretreatment with 1,2-diazole does not affect superoxide dismutase (SOD), catalase (CAT), serum urea and creatinine level during nephrotoxicity when compared to cisplatin-induced group. Moreover, the 1,2-diazole animal's shown significant decrease in urine volume and kidney weight when compared with cisplatin-induced group. Histopathological findings reveals the protective efficacy of 1,2-diazole that restores histopathological changes against nephrotoxicity.

Conclusion: These analyses will provide a critical evidence that 1,2-diazole could provide a new protective strategy against cisplatin-induced nephrotoxicity.

Key words:
1,2-diazole, pyrazole, cisplatin, nephrotoxicity, antioxidant, renal disorder, Rhizophora apiculata, mangroves