

Abstract

In the present study, the effects of three antioxidants namely hesperidin, thymoquinone and quercitrin on several parameters related to cisplatin-induced nephrotoxicity and hepatotoxicity in rats were studied in comparison with silymarin. The antioxidant drugs were given for normal as well as cisplatin-treated rats. Drugs were given for 7 days starting one day before cisplatin injection. The effects of the test drugs were estimated on serum creatinine and BUN levels, serum ALT and AST activities and serum TG and TC levels. Furthermore, the effect of test drugs was studied on kidney and liver contents of MDA, GSH and NO. Histopathological examination of both kidney and liver tissues was done. In addition, western blot analysis was done to determine the effect of cisplatin and test drugs on *NF- κ B* and phosphorylated *Akt* expression levels in kidney and liver tissues. In addition, an *in vitro* experiment was done to detect the effect of test drugs on the anticancer activity of cisplatin when combined with it on two different cell lines namely human breast adenocarcinoma (MCF-7) and human hepatocellular carcinoma (HepG-2) using MTT assay. Results showed that test drugs significantly reduced cisplatin-induced elevations in serum Cr, BUN levels, ALT and AST activities, TG and total cholesterol levels. They also reduced cisplatin-induced oxidative stress by significant reduction in kidney and liver MDA and NO content and elevation of GSH content. In addition, test drugs significantly reduced cisplatin-induced increased *NF- κ B* expression and decreased p-Akt expression in both kidney and liver. The histopathological examination revealed that test drugs greatly protected kidney and liver against cisplatin-induced injury. Hesperidin, thymoquinone & quercitrin could be promising agents for clinical use as nephro and hepato protection against cisplatin-induced nephrotoxicity and hepatotoxicity. Their effects were similar to that of silymarin.