

Carbocisteine Reduces the Cytotoxicity of Oxaliplatin

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Hepatic injury induced by oxaliplatin has been reported. Even though agents are available that reduce oxaliplatin-induced hepatocyte toxicity, their mode of action has remained obscure. In the present study, hepatic L02 cells were incubated with different combinations of oxaliplatin and carbocisteine. Significantly increased levels of reactive oxygen species (ROS) were found in L02 cells treated with oxaliplatin. Using 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2*H*-tetrazolium (MTS) as an indicator of cell viability and flow cytometry, we found that carbocisteine could reverse oxaliplatin-induced apoptosis of L02 cells. Western blot analysis demonstrated that oxaliplatin could induce apoptosis of L02 cells by reducing the Bcl-2/Bim ratio, stimulating the cytochrome c release, and activating caspase-3. All of these effects could be suppressed by carbocisteine. We further found that carbocisteine did not affect the anticancer effect of oxaliplatin against HT-29 cells. This is the first report opening prospects for the clinical use of carbocisteine in the pretreatment against liver injury accompanying the chemotherapy regimen with oxaliplatin.

Key words: Carbocisteine, Oxaliplatin, Hepatic Injury