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Abstract

Morphological Value of Nephrotoxic Effects of Doxorubicin and PLGA-Doxorubicin †

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Abstract: Doxorubicin (DOX) is a chemotherapy drug that causes nephrotoxicity in rodent models and, to a lesser extent, in cancer patients. Doxorubicin hydrochloride or doxorubicin-loaded poly(lactide-co-glycolide acid) (Dox-PLGA) nanoparticles at a therapeutic dose were injected intravenously into male Wistar rats. PLGA is a biodegradable polymer used as a drug delivery vehicle. However, the therapeutic effect of Dox-PLGA is not clearly understood. The aim of the study is to estimate a comparative assessment of the nephrotoxic effects of different forms of doxorubicin. This investigation was carried out on male Wistar rats weighing about 200–250 g (n = 24). Morphological assessment of the kidneys was performed using light microscopy. Ultrastructural changes were studied using a TEM Libra120 transmission electron microscope. The levels of ALT, AST, urea, and creatinine in blood serum were determined. Comparison of digital data between experimental groups was performed using the Kruskal–Wallis test (ANOVA). Differences were considered statistically significant at $p < 0.05$. Degeneration changes in the proximal tubules with the destruction of the brush border were revealed by light and electron microscopy in the kidneys on the 8th and 21st days of the experiment after the administration of doxorubicin hydrochloride and its nanosomal form Dox-PLGA. It was found that on the 8th day, PLGA-doxorubicin causes less pronounced degenerative changes in the epithelium of the proximal tubules. The short-term effect after administration of Dox-PLGA is characterized by an increase in creatinine levels, and the long-term effect by an increase in the level of ALT activity, as well as the concentration of urea and creatinine.

Keywords: nephrotoxicity; doxorubicin; PLGA; nanoparticles; toxic effect; morphology; biochemistry

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