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APOPTOSIS IN HEPATOCELLULAR CARCINOMA-29 CELLS AFTER LITHIUM CARBONATE ADMINISTRATION *IN VIVO*

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Hepatocellular carcinoma (HCC) is characterized as an extremely heterogeneous and malignant type of liver cancer, the development of HCC is accompanied by genetic mutations in the signaling pathways involved in the cell proliferation, growth and death. It was shown that lithium salts can stimulate apoptosis in various cancer cells; therefore, the aim of this study was to estimate the ability of lithium carbonate to affect on the development of apoptosis in hepatocellular carcinoma-29 (HCC-29) cells *in vivo*. By light and transmission electron microscopy, it was shown that typical morphological features of apoptosis develop in HCC-29 cells after administration of 20 mM lithium carbonate intramuscularly along the periphery of the tumor every day. By immunofluorescence, it was found that lithium significantly increased both of caspase-3 and the pro-apoptotic protein Bad levels, and decreased the anti-apoptotic protein Bcl-2 levels. These results indicate that lithium carbonate induces apoptosis in HCC-29 cells *in vivo*. The combined use of lithium carbonate and chemotherapeutic drugs can allow targeted effects on various cellular signaling pathways in HCC cells to enhance pro-apoptotic drug potential and overcome the resistance of tumor cells to apoptosis.

Keywords: hepatocellular carcinoma-29, lithium carbonate, morphology, apoptosis