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The Determination of Cytostatic Activity on a 3D Spheroids-Based Model in Comparison with Conventional Monolayer Culture

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It is becoming approved that screening of compounds on a platform applying two-dimensionally (2D)-cultured cell lines is incapable to precisely predict clinical activity of drugs; therefore three-dimensional (3D)-culture systems are emerging and show potential for better simulating the physiological cell microenvironment. In this regard, a 3D models that reflect all types of intercellular interactions, as well as the interaction of cells with the extracellular ma-

trix, are becoming increasingly accepted. Spheroids represent one of these models. The purpose of our study was to reveal the antiproliferative and cytotoxic activity of cisplatin, doxorubicin, fluorouracil, and etoposide on Vero CCL-81 and HEK293 cell lines under 2D (monolayer) and 3D (spheroids) culture conditions. The comparison of antiproliferative activity (IC_{50}) and cytotoxic activity (CC_{50}) obtained in different culture conditions revealed that the antiproliferative activity of compounds was higher in 2D while cytotoxic effect was more prominent in 3D. We suggest that cells in 3D are cultured in more physiological conditions, consequently they are more resistant to antiproliferative activity of compounds. More prominent cytotoxic effect in 3D allowed us to theorize that implementation of 3D spheroids-based model will allow to recognize early toxicity at the initial steps of preclinical studies in vitro. Our data approved that in the course of determination of compounds specific activity, cell type, the cell proliferation rate and in the optimal diameter of spheroids for each cell type should be taken into account.

Keywords: spheroids, monolayer, drugs, antiproliferative activity, cytotoxicity