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CYTOTOXIC AND APOPTOTIC FUNCTIONS OF LICOFELONE ON RAT GLIOMA CELLS

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Gliomas are the largest group of central nervous system tumors and despite of clinical treatments death rate is very high. Inhibition of both cyclooxygenase and lipoxygenase pathways that take role in arachidonic acid metabolism prevents cancer development and induces apoptosis. One of the most promising compounds that blocks both of these pathways is licofelone. Using colchicine and 5-fluorouracil as positive controls, we questioned whether licofelone affects the survival of rat glioma cell line (C6) and induces apoptosis *in vitro*. After growing the cells in culture, we determined viability with MTT, apoptosis with flow cytometry and activity of caspase enzymes with real time PCR. All used doses of colchicine and 5-fluorouracil were cytotoxic and reduced the number of surviving C6 cells as much as 44% and 60%, respectively. Comparing to the control, treatments with 10, 50 and 100 μM licofelone for 24 or 48 h did not influence C6 survival, however, 150, 200 and 250 μM licofelone reduced the number of living cells by 58, 88 and 93%, respectively, and induced apoptosis of C6 cells in a dose and time dependent manner. Licofelone did not change the level of caspase-9, but increased the level of caspase-3. Comparing with 5-fluorouracil and colchicine, the present study reveals for the first time the possibility that licofelone possesses a strong dose and time dependent antiproliferative and proapoptotic properties on glioma cells.

Keywords: Antiproliferative effects – apoptosis – arachidonic acid – glioma-licofelone

INTRODUCTION

Formed by glial cells, gliomas comprise the largest group of the central nervous system (CNS) tumors and infiltration with gliomas leads to neurological dysfunction and eventually death. High incidence and malignity of glioblastoma multiform, the most common form of gliomas, have led scientists to work hard to better understand and treat these tumors [20, 38]. Despite all the efforts (radio-, chemo- and gene-therapy), there has been almost no change in the progress of curing primary malignant brain tumors in the last 30 years [12, 18]. Therefore, new cellular transduction pathways should be defined as putative targets for the management of gliomas [27, 32]. Two of these may be cyclooxygenase (COX) and lipoxygenase (LOX) pathways of arachi-

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