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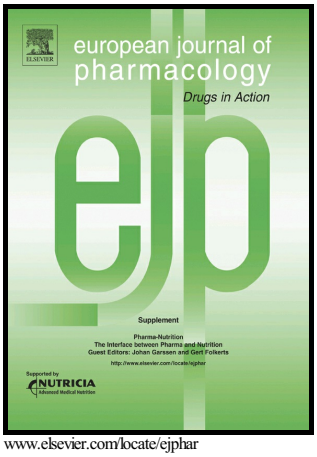

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In vitro characterization of alkylaminophenols-induced cell death

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ABSTRACT

Alkylaminophenols are synthetic derivatives well known for their anticancer activity. In the previous studies, we described the activity of the series of Alkylaminophenols derivatives and their ability to induce cell death for many cancer cell lines. However, temporal heterogeneity in cell death induced by lead compounds, N-(2-hydroxy-5-nitrophenyl (4'-methylphenyl) methyl) indoline (Compound I) and 2-((3,4-dihydroquinolin-1(2H)-yl) (4-methoxyphenyl) methyl) phenol (Compound II), has never been tested on osteosarcoma cells (U2OS). Here, we address the level of cell-to-cell heterogeneity by examine whether differences in the type of compounds could influence its effects on cell death of U2OS. Here, we applied imaging, computational methods and biochemical methods to study heterogeneity, apoptosis, reactive oxygen species and caspase. Our results demonstrate that the Hill coefficient of dose-response curve of Compound II is greater than compound I in treated U2OS cells. Both Compounds trigger not only apoptotic cell death but also necro-apoptotic and necrotic cell death. The percentage of these sub-populations varies depending on compounds in which greater variance is induced by compound II than Compound I. We also identified the accumulation of compounds-induced reactive oxygen species during the treatment. This resulted in caspase 3/7 activation in turn induced apoptosis. In summary, the screening of Compound I and II molecules for heterogeneity, apoptosis, reactive oxygen species and caspase has identified compound II as promising anti-osteosarcoma cancer agent. Compound II could be a promising lead compound for future antitumor agent development.