Abstract:

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1 to 2 cases per 100,000 adults. Caffeine as a natural substance can have anti-cancer effects by reducing cell proliferation and inducing apoptosis. On the other hand, nanocarriers can be used as an efficient method for the proper delivery of drugs at the site of tumors, stability and protection of drugs, targeting specific organs and long shelf life. The aim of this study was to investigate the anticancer effects of caffeine nanoemulsion and free caffeine on K562 cell line as a blood cancer cell line. For this purpose, nanoparticles were produced using spontaneous water-in-oil emulsion method using lecithin and Tween 80, and the physicochemical properties and stability of the produced nanoemulsion were investigated. Then K562 cancer cells were treated with different concentrations of caffeine nanoemulsion (0,100, 200, 400, 600, 800 and 1000 ug/ml) and free caffeine (0,100, 200, 400, 600, 800 and 1000 ug/ml) and the cytotoxicity of the produced nanoemulsion was evaluated using neutral red, MTT and trypan blue methods, as well as the amount of apoptosis and necrosis with acridine orange/propidium iodide staining method. Nanoparticles with a size of 168 ± 1.03 nm were produced in the form of spherical particles, with a smooth surface and a uniform size of 0.18, encapsulation efficiency of 76 ± 0.8%, negative zeta potential of 30 mv, stable and controlled release. . Studying the stability of nanoemulsions produced for 2 months at temperatures of 4 and 25 degrees Celsius showed high stability with minimal changes in the physicochemical properties of nanoparticles. The results of the cytotoxicity tests (MTT, neutral red and trypan blue) showed that the decrease in the viability of cells treated with different concentrations of caffeine nanoemulsion and free caffeine was dependent on concentration and time, and caffeine nanoemulsion was Compared to free caffeine, it has more cytotoxic effects on K562 cancer cells. IC50 obtained based on MTT test for caffeine nanoemulsion 434.78±3 ug/ml after 24 hours, and 285.71±3 ug/ml after 48 and for free caffeine 816.32±4.5 ug/ml after 24 hours and 555.23±1.7 ug/ml after 48 hours. The results of the neutral red and trypan blue tests also showed the same concentrations as the MTT test as IC50. Morphological evaluation of cancer cells treated with caffeine nanoemulsion and free caffeine showed effects of apoptotic cell death, including nuclear shrinkage and cytoplasmic bubbles. and the number of living cells was greatly reduced. The results of the

acridine orange/propidium iodide staining test (cell nucleus morphology evaluation) also showed that the percentage of apoptotic and necrotic cells in cultures exposed to caffeine nanoemulsion was significantly higher than free caffeine. Of course, the mechanism of cell death caused by caffeine nanoemulsion and free caffeine was more of apoptosis than necrosis. In general, the results of this research indicated a decrease in survival and induction of apoptosis in K562 cells as a chronic myeloid leukemia cancer cell line after exposure to caffeine nanoemulsion, and caffeine nanoemulsion can be used as an auxiliary method. Along with other treatment methods in the treatment of chronic myeloid leukemia cancer, he suggested after further studies.

Keywords: Chronic myeloid leukemia, caffeine, nanoemulsion