Study of the effect of nanofiber scaffolds loaded with oleuropein on the induction of autophagy in 5-fluorouracil-resistant MKN-45 cells

Abstract

Background: Gastric cancer is one of the most common and deadly cancers in the world. The stomach is located in the digestive tract between the esophagus and the small intestine, and helps digestion by secreting enzymes, stomach acid, and vitamin B12 absorption factor. The stomach consists of epithelial cells and glands that are covered with a mucous membrane. One of the usual and conventional methods in the treatment of cancer by chemotherapy is the use of 5-fluorouracil, which is an analogue of uracil, and upon entering the cell, it converts into its active forms, which include fluorodeoxyuridine monophosphate (FdUMP), fluorodeoxyuridine tri Phosphate (FdUTP) and fluorouridine triphosphate (FUTP) have been converted and these active forms prevent the synthesis and repair of RNA and DNA by inhibiting the enzyme thymidylate synthase, as an enzyme for making pyrimidines, and subsequently prevent protein synthesis. A main compound in olives is 3-4 dihydroxyphenyl ethanol-allenolic acid, which is known as Oleuropein.

Aim*:* The aim of this study is to investigate the effect of nanofibrous scaffold loaded with Oleuropein on the induction of programmed death in MKN-45 cells resistant to 5-fluorouracil.

Materials and Methods: After purchasing the MKN-45 cell line, transferring it to the culture medium inside the flask and passaging several series of cells in the logarithmic phase were used. The expression level of apoptosis-inducing genes (Bax, P53) and anti-apoptotic gene (Bcl-2) was investigated using real-time PCR method in MKN-45 cells resistant to 5-FU in vitro.

Results: In this study, PCL-PEG nanofiber scaffold was used to load oluropin drug and create a platform for cell growth and proliferation. According to the

results of the MTT test on the third day after the treatment, the release of the drug from the scaffold is carried out from the third day onwards, and the effect of the drug on the cells can be confirmed in the 7-day MTT test. Also, according to the results of MTT, the combination of two drugs 5-fluorouracil and oluropine loaded in PCL-PEG scaffold showed higher cytotoxic activity than other groups.

Conclusion: The results of this study showed that the combination of 5-fluorouracil and simvastatin in the PCL-PEG nanofiber scaffold has the potential to inhibit the growth of cancer cells resistant to 5-fluorouracil and can be considered as a suitable approach for the treatment of gastric cancer.

Key words: : 5-fluorouracil- oluropine- gastric cancer- resistant- nanofiber scaffolds- LC3 cell Beclin-1