Study of the effect of nanofiber scaffolds loaded with oleuropein on the induction of apoptosis 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. 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.

Aim: Here, we examined the effect of the scaffold containing the bioactive substance Oleoreupien on the expression of apoptotic pathway genes (Bax, Bcl-2 and P53) in MKN-45 cells resistant to 5-fluorouracil and comparing it with the control group

Materials and Methods: After purchasing the MKN-45 cell line, transferring it to the culture medium inside the flask and passing 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: According to the calculations, the level of BAX and P53 gene expression in cells treated with scaffolds containing oluropine shows a significant increase compared to other group. And the expression level of Bcl-2 in this group has also decreased significantly compared to other group. The increase of Bax and P53 and the decrease of Bcl-2 is the reason for the increase in apoptosis in resistant cells treated with oluropine and 5-fluorouracil.

Conclusion: The results of this study showed that the combination of Oleoreupien 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.

Keywords: Gastric Cancer,Oleoreupien,5-Flurouracil, Nanofiber Scaffolds,Drug Resistant,Apoptosis,p53,Bax,Bcl-2