Cancer is a devastating disease that causes great losses in worldwide. The increasing incidence of cancer is necessitating the development of new clinical approaches against this relentless disease. There is a huge interest to development of combined therapies that can provide both decreased the side effects and increased the effect at lower doses of chemotherapeutics. Among men and women, lung cancer and breast cancer have the highest incidence, respectively. Apoptosis is programmed cell death and several genes such as p53, Bcl-2, Bax, and mTOR are involved in regulation of apoptosis. Cisplatin is a chemotherapy drug used in the clinical treatment of many cancer types such as breast, bladder, lung, cervical cancers and it has significant side effects. Gallic acid (GA), 3,4,5-trihydroxylbenzoic acid, is a phenolic compound that abundant in plant sources such as fruits and green tea. Gallic acid has anticancer potential, but studies which exhibite the molecular effect mechanism of this compound in combination with cisplatin are limited in the literature. This study is aimed to investigate the antiproliferative, apoptotic and antivasculogenic effects of gallic acid on human non-small cell lung cancer cell line (A549) and breast cancer (MCF-7) cell line and their synergistic activities with cisplatin.

A549 and MCF-7 cells were treated with gallic acid and cisplatin combination and antiproliferative effects were examined by WST-1 and clonogenic assay. To examine apoptotic effects, Cell Death Detection Elisa assay was performed and Human VEGF Elisa method was used to determine the amount of VEGF in vitro. p53, Bax, Bcl-2, mTOR and PTEN gene expression levels were measured by RT-qPCR. β-actin was used for optimization as housekeeping gene. Each experiment was performed in triplicate.

The combination of cisplatin and gallic acid decreased cell viability in both cell lines depending on the combination rate. The increase in apoptosis as a result of treatment with IC50 doses was found 7.3 and 5.7 fold in A549 and MCF-7 cell lines, respectively. The amount of VEGF which optimized in the control group as 100 pg/ml, determined as 65.9 pg/ml in A549 cells and 73.1 pg/ml in MCF-7 cells. In both cell lines, the combination of cisplatin and gallic acid significantly increased the expression of apoptotic p53 and Bax genes, also this combination significantly reduced antiapoptotic Bcl-2 and mTOR genes expression levels compared with the control group (p<0.0001). There were no significant changes in PTEN expression levels. The antiproliferative and apoptotic effects of cisplatin, may be increased by combination with gallic acid and be synergistically enhanced in some cancer types.

Keywords: PTEN, Cell viability, VEGF, Gallic acid, Lung cancer