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The effects of thymoquinone on small cell lung cancer cell lines

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Abstract
Lung cancer is one of the most common types of cancer that causes death. Small cell lung cancer seen in 14%, is a type of cancer that is closely related to smoking and has an aggressive course. It is a metastatic tumor when diagnosed. In this stage where surgical treatment cannot be performed, the primary treatment is chemotherapy. Cisplatin is amongthe options in chemotherapy combinations. In vivo and in vitro studies have shown the antitumoral and antineoplastic effects of the bioactive component thymoquinone obtained from the Nigella Sativa plant. Therefore, our study aimed to target the effects of thymoquinone and cisplatin on small cell lung cancer cell lines. Small cell lung cancer cell lines were cultured in accordance with international standards. The cells were treated with 100 µM thymoquinone and 200 µM cisplatin for 4h under incubation conditions. We used dimetil sülfoksit (DMSO) for negative control (thymoquinone and cisplatin solved in DMSO). Experiments were repeated 4 times in the same laboratory, by the same person, at different times. In conclusion, the effects of thymoquinone and cisplatin were statistically significant at 10,100,200 µM concentration compared with DMSO separately. The effective concentration of thymoquinone was detected to be at a concentration of 100 µM, and that of cisplatin at a concentration of 200 µM. 100 µM thymoquinone is more effective and statistically significant than both 100 µM and 200 µM cisplatin. 200 mM thymoquinone is more effective than 200 µM cisplatin.

Keywords: thymoquinone, lung cancer, cisplatin, cell lines

Introduction
Lung cancer is one of the most common types of cancer that causes death. Non-small cell lung cancer (NSCLC) accounts for 75% of all lung cancers. Small cell lung cancer (SCLC), which is seen in 14%, is a type of cancer that is closely related to smoking and has an aggressive course. At the time of diagnosis, 60% of SCLC and 40% of NSCLC are Stage 4 metastatic tumors [1, 2]. In this stage where surgical treatment cannot be performed, the primary treatment is chemotherapy. Cisplatin is among the options in chemotherapy combinations [3]. In vivo and in vitro studies have shown the antitumoral and antineoplastic effects of the bioactive component thymoquinone obtained from the Nigella Sativa plant [4,5,6]. Therefore, our study aimed to target the effects of thymoquinone and cisplatin on small cell lung cancer cell lines.

Method and Materials
ATCC (American Type Culture Collection) NCI-H1048 CRL-5853 numaralı küçük hücreli akciğer kanseri hücre hattı üzerinde çalışmamız gerçekleştirilmiştir (figure 1). Cancer cells were cultured in RPMI supplemented with 10% fetal bovine serum (FBS; Gibco, USA), %1 antibiotic (Gibco, USA) and DMEM (dimetil sülfoksit) with same supplemented at 37°C, %5 CO_2 [7]. Cell line was used for evaluated potential effect of thymoquinone. In our previous works cell viability has been assessed using MTT (3-(4, 5-dimetiltiazol-2-il) 2, 5-difenil tetrazolyum bromid) assay. According to the results ED50 concentration of thymoquinone have been determined as 100 µM and cisplatin as 200 µM. Cells were cultured for 24 h in 96 well plates (2500/ml cells) in 10% FBS RPMI appropriate medium. Before chemical exposure, the media was replaced with serum free medium for 16h. The cells were treated with 100 µM thymoquinone and 200 µM cisplatine for 4h under incubation conditions (figure 2). We used DMSO (dimetil sülfoksit) for negative control (thymoquinon and cisplatin solved in DMSO). Experiments were repeated 4 times in the same laboratory, by the same person, at different times.

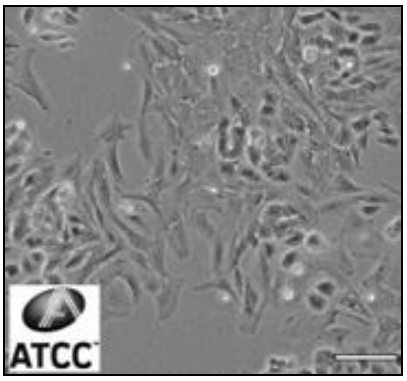

Fig 1: NCI-H1048 CRL-5853 cell line image

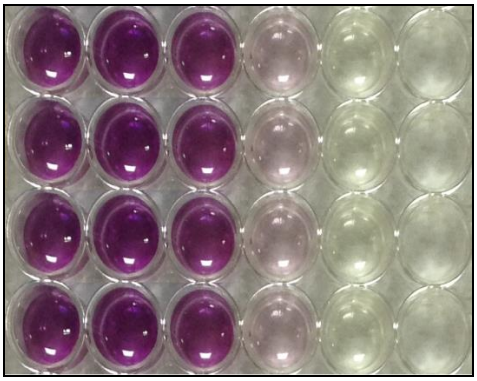

Fig 2: Chemical treatment under incubation image

Results

In CRL-5853 cell line; the effects of thymoquinone and cisplatin were statistically significant at 10,100,200 µM concentration when compared with DMSO separately ($p<0.001$). The effective concentration of thymoquinone was detected to be at 100 µM, and that of cisplatin at 200 µM, and thymoquinone at 200 µM was found to be a toxic concentration. At 10 µM concentration, cisplatin is more effective than thymoquinone ($p<0.05$). However, is concentration is not the effective of both chemicals. 100 µM thymoquinone is more effective and statistically significant than both 100 µM and 200 µM cisplatin ($p<0.001$). 200 mM thymoquinone is more effective than 200 µM cisplatin ($p<0.001$). However, the toxic concentration of thymoquinone is the effective Concentration of cisplatin (table 1).

BEAS-2B cell line is a normal bronchial cell and has been studied for control studies. No statistically significant difference was found between thymoquinone and cisplatin at 10 and 100 µM concentrations. Thymoquinone at 200 µM concentration was toxic in BEAS-2B cell lines ($p<0.05$ and table 2).

As a result, thymoquinone was found to be more effective than cisplatin at effective concentrations of chemicals in small cell lung cancer cell lines.

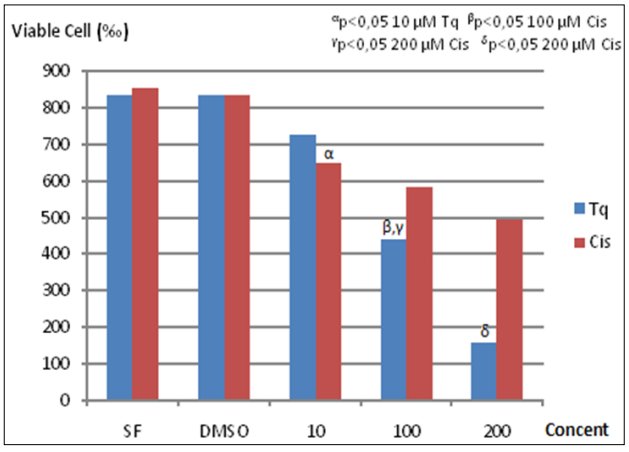

Fig 3: Statistical analysis of Tq and Cis in NCI-H1048 CRL-5853 cells

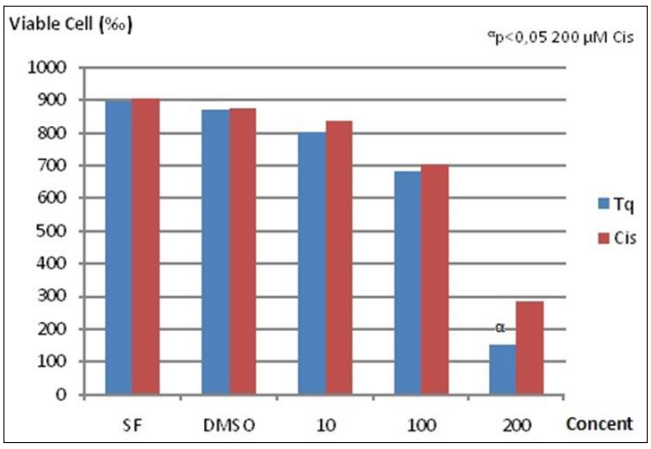

Fig 4: Statistical analysis of Tq and Cis in BEAS-2B cells

Discussion and Conclusion

SCLC is an aggressive neuroendocrine cancer associated with smoking. Patients usually present with short-term symptoms and 60-65% of metastatic disease. It is heterogeneous in response to chemotherapy. There are surgical treatment options in stages 1 and 2. A combination of cisplatin etoposide is used in the treatment of the limited stage. In extensive disease, etoposide is combined with cisplatin agents [8]. Despite all the treatments, unfortunately, the prognosis is poor. In our study, comparison with cisplatin, which is often used in combination in chemotherapy was preferred. Thymoquinone, the bioactive component of Nigella Sativa; anticarcinogenic, antitumoral, antiulcerogenic, antibacterial, analgesic, antioxidant, hypoglycemic and immune system enhancing effects have been reported [9, 10, 11]. Therefore, in our study, the effects of thymoquinone on small cell lung cancer cell line were targeted. Concentrations that cause death of 50% (EC50) of cancer cells in cell culture; were detected at concentrations of 100 µM for thymoquinone and 200 µM for cisplatin. The effects of thymoquinone and cisplatin were statistically significant at 10,100,200 µM concentration compared with DMSO separately. The toxic concentration of thymoquinone was detected to be at a concentration of 200 µM. 200 mM thymoquinone is more effective than 200 µM cisplatin but this concentration is an effective concentration for cisplatin, it is a toxic concentration for thymoquinone. It was determined that the effective concentration of thymoquinone (100 µM) more effective than both 100 µM cisplatin concentration and 200 µM (effective concentration).

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Ethical approval and competing interest

The study has been carried out on cancer cell lines in the cell culture laboratory and accordance with international standards.

All authors declared that there is no conflict of interest.

Availability of data
All data obtained in our study are recorded and available.

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