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NOVEL METHODS AND EMERGING TARGETS IN
DRUG DISCOVERY & PATENTED DRUG DEVELOPMENT



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Comparative effects of monotherapy and polytherapy with CAPE and Cisplatin on SKBR3 Breast cancer cell lineOnur EROGLU^a, Esin GÜVENİR ÇELİK^a, Hacer KAYA^a, Kübra ERDOĞAN^a, Büşra SEVİM^a, Merve BAŞOL^a^aBilecik Şeyh Edebali University, Faculty of Science and Letters, Department of Molecular Biology and Genetics, Bilecik/TurkeyE-mail: onur.eroglu@bilecik.edu.tr

Background: Cancer treatment includes many strategies and chemotherapy still plays a central role. Cisplatin(Cis) is a widely used chemotherapeutic agent. It has been used for treatment of numerous human cancers including bladder, head and neck, lung, ovarian, and testicular cancers. (1) Cisplatin kills cancer cells by binding to DNA and interfering with its repair mechanism. Combination therapy of cisplatin with other cancer drugs have been applied as novel therapeutic strategies for many human cancers. Caffeic acid phenethyl ester (2-phenylethyl (2E)-3-(3, 4-dihydroxyphenyl) acrylate; CAPE) is a polyphenolic compound present in honey and propolis of honeybee hives. CAPE is known to possess various pharmacologic activities such as antioxidant, antiviral, immunomodulatory, anti-inflammatory and anticancer effects(2). The aim of the present study was to investigate the effects of monotherapy and polytherapy of CAPE and cisplatin on SKBR3 breast cancer cell line.

Methods: SKBR-3 cells were cultured in DMEM supplemented with 10% fetal bovine serum (FBS) in a humidified atmosphere of 5% CO₂ at 37 °C respectively. Cell viability was determined by MTT assay that assess the relative percentage of metabolically active cells compared to untreated cells. For MTT assay the dosage range of cisplatin is 30-90 µM and CAPE 30-75 µM and different dosage of two drugs .The IC₅₀ (concentration that inhibits 50% of cell growth) was calculated for any drugs and combination with CAPE and Cisplatin. To determine cytotoxic effect of drugs a combination was used for survival assay for 24 h, 48 h and 72h.

Results: We compared the effect of monotherapy and polytherapy of drugs on breast cancer cell line with the control group. We observed the amount of cell viabilities after drug treatment were 54,86% for 90µM CAPE, 53,98% for 40µM Cisplatin and 77% for 20 µM CAPE+10 µM Cisplatin combine treatment. CAPE and Cis single therapy was shown decrease in viable cells at 24 h. We found in this study, a decrease of metabolic activity of the cell line with treatment CAPE and Cisplatin. We detected that the cytotoxic effect of these drugs with combine treatment(CAPE+Cis) are less than a single treatment on growth assay.

Conclusions: These results show that polytherapy is more effective than monotherapy because cancer cells may less to have resistance to multiple drugs treatment and this approach increases the chance of effective treatment.

Keywords: CAPE, cisplatin, breast cancer, polytherapy

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Investigation of the Effects of 5-Fluoruracil and Temozolomide Combinations on Cell Survival in SKBR3 Human Breast Cancer Cell LineOnur EROGLU^a, Esin GUVENİR CELİK^a, Hacer KAYA^a, Kubra ERDOGAN^a, Busra SEVİM^a, Merve BASOL^a^a Bilecik Şeyh Edebali University, Faculty of Science and Letters, Department of Molecular Biology and Genetics, Bilecik/TurkeyE-mail: onur.eroglu@bilecik.edu.tr

Background: Breast cancer is a malignant tumor that begins in breast cells. This malignant tumor can invade different tissues in different regions of the body. Breast cancer is one of the most common types of cancer worldwide [1]. Temozolomide (TMZ) is widely used in Glioblastoma multiforme therapy because it can easily pass through the blood barrier due to its small structure. 5-Fluoruracil (5-FU) is a water-soluble, acidic, hydrophilic drug and is frequently used in the treatment of brain tumors [2]. The aim of this study is to investigate the cytotoxicity effects and cell proliferation of using single drug and a combination of 5-Fluoruracil and Temozolomide in SKBR3 breast cancer cell line.

Methods: SKBR3 breast cancer cell line was cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing Fetal Bovine Serum (FBS) 10% (v/v) and penicillin streptomycin 1% (v/v) and incubated at 37°C in a humidified 5% CO₂ incubator. Drug doses were determined by MTT assay. For cell viability, cells were treated with IC₅₀ (concentration resulting in 50% inhibition of control growth) value for 24 h, 48 h and 72h of incubation.

Results: Only 5-FU produced an IC₅₀ of 50 µM, whereas only TMZ resulted in an IC₅₀ of 80 µM in the SKBR3 cell line. Especially, concentration of combination group 50 µM for 5FU- 80 µM for TMZ. 5-FU and TMZ combination therapy is more effective than single therapy of these drugs. 5-FU and TMZ single therapy was showed decrease in viable cells at time dependently. We observed that the cytotoxic effects of these drugs are decreased significantly with 5-FU and TMZ combined treatment at 48 hours.

Conclusions: These results indicated that cell viability decreased treatment with 5-FU and TMZ together compared to single using 5-FU and TMZ treatment in SKBR3 breast cancer cell. The findings are highly important in terms of annihilation of the cytotoxic effects through combined therapy and the fight against cancer.

Keywords: Breast cancer, SKBR3, 5-fluoruracil, Temozolomide

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