4th INTERNATIONAL BAU DRUG DESIGN CONGRESS

4. ULUSLARARASI BAU İLAÇ GELİŞTİRME KONGRESİ

BAU TIP

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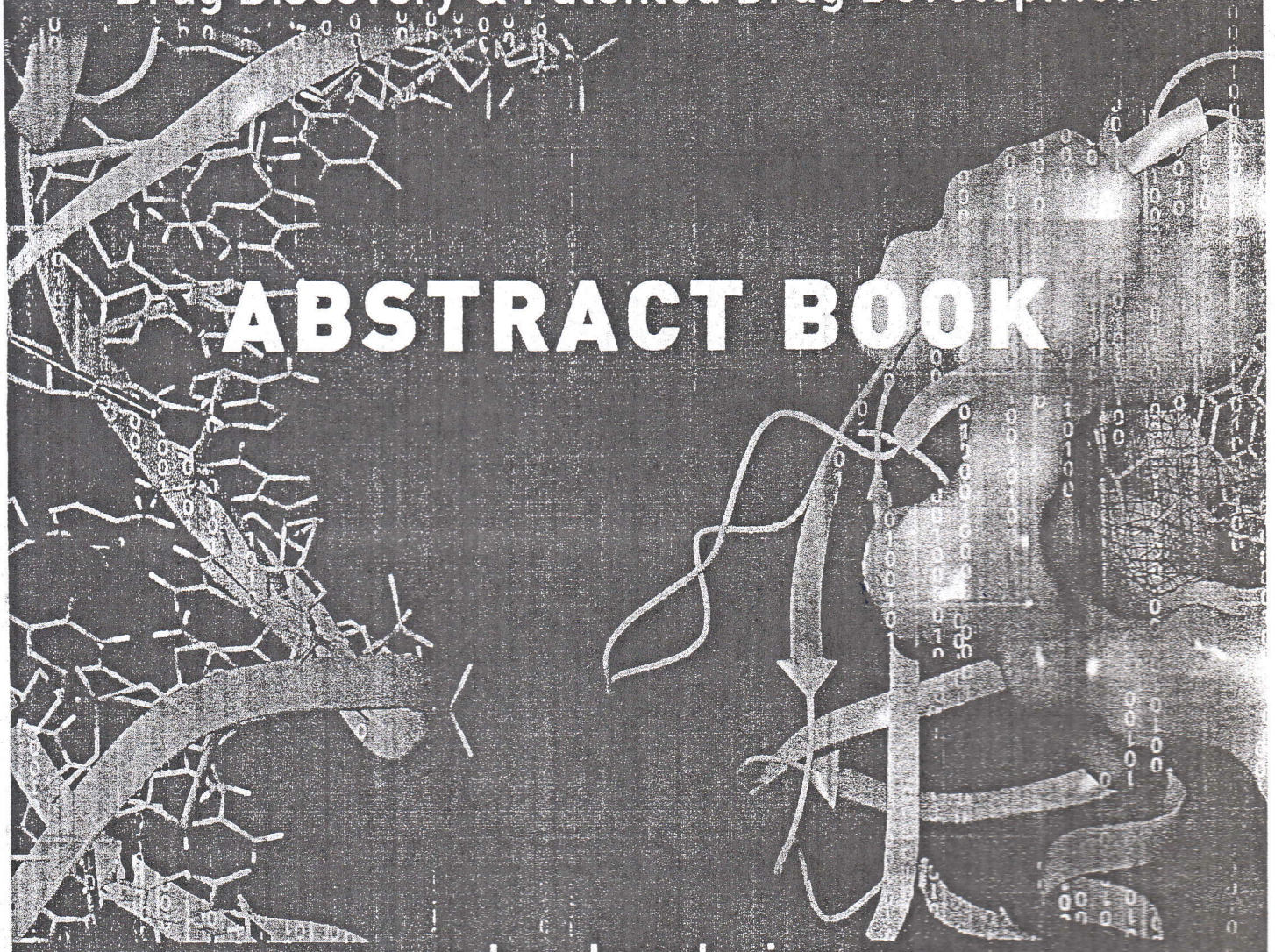
BAHÇEŞEHİR UNIVERSITY SCHOOL OF MEDICINE ISTANBUL TURKEY

Novel Methods and Emerging Targets in Drug Discovery & Patented Drug Development



ABSTRACT BOOK

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References:

1. a) Broccolo F, Cainelli G, Caltabiano G, Cocuzza C E A, Fortuna C G, Galletti P, Giacomini D, Musumarra G, Musumeci R, Quintavalla A J. (2006) ***Med. Chem.***; 49: 2804. b) Halve A K, Bhadauria D, Dubey R. (2007) ***Bioorg. Med. Chem. Lett.***; 17: 341.
2. a) Srivastava S K, Srivastava S, Srivastava S V. (2002) ***Ind. J. Chem.***, 41B: 2357-2363. b) Desai K G, Desai K R. (2006) ***Bioorg. Med. Chem.***, 14: 8271-8279.

PP-57 Investigation of Cytotoxic Effect of Doxorubicin, 5-Fluorouracil, Propranolol and Triple Combined Treatment in MCF-7 Breast Cancer Cell Line.

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Background: For some cancers, chemotherapy drugs are most effective when given in combination. Because single-agent treatment often results in cytotoxic effect due to the high dose. The purpose for combination chemotherapy is to use drugs that work by different mechanisms, therefore reducing the possibility that cytotoxic effect will develop (1). Doxorubicin acts in the cancer cell intercalation into DNA and corruption of topoisomerase-II-mediated DNA repair and generation of free radicals and their damage to cellular membranes, DNA and proteins (2). Anti-metabolite drugs function by inhibiting basic biosynthetic processes, or by being included into macromolecules, such as DNA and RNA, and inhibiting their normal function (3). 5-fluorouracil (5-FU) does one of them. In a study, it showed that results of combining chemotherapeutic drugs, such as 5-FU with propranolol at the lowest effective concentration in synergistic or antagonistic effects on cell proliferation *in vitro* depending on the cell type and used the dose of chemotherapy (4). Furthermore, in this study, we aimed to decrease the cytotoxic effects of these drugs in a single treatment. So we treated triple combination of these drugs in literature for the first time.

Methods: MCF-7 breast cancer cell line was cultured and maintained in RPMI medium including with 10% (v/v) fetal calf serum and 1% (v/v) penicillin/streptomycin, at 37˚C in a humidified atmosphere containing 5% carbon dioxide. MTT assay was performed to evaluate the effects of different concentrations of Doxorubicin, 5-Fluorouracil, Propranolol and triple combination of these drugs for 24 h. To determine the cytotoxic effect of drugs combination was used in survival assay. After the incubation, cells were treated with Doxorubicin, 5-Fluorouracil, Propranolol and triple combination. After drug treatment, cells were counted with Naubauer hemocytometer 24 h and 48 h.

Results: We observed that IC_{50} values 0.01 mg/ml for doxorubicin, 3 mg/ml for 5-FU, 30 mg/ml for propranolol and 0.2/1/30 mg/ml for respectively doxorubicin, 5-FU and propranolol combination by MTT assay. We detected that cytotoxic effect of these drugs with triple treatment are less than single treatment on growth assay.

Conclusions: The recent studies revealed that triple combination therapy was a potential candidate for chemotherapy. In this study triple combination of doxorubicin, 5-FU and propranolol are treated for the first time in literature. Thus cytotoxic effect of these drugs with triple treatment can be reduced more than single treatment. In future, understanding the mechanism of these drugs of combination will assist the clinic studies.

Keywords: *Doxorubicin, 5-Fluorouracil, Propranolol, Breast Cancer, Combine Therapy*

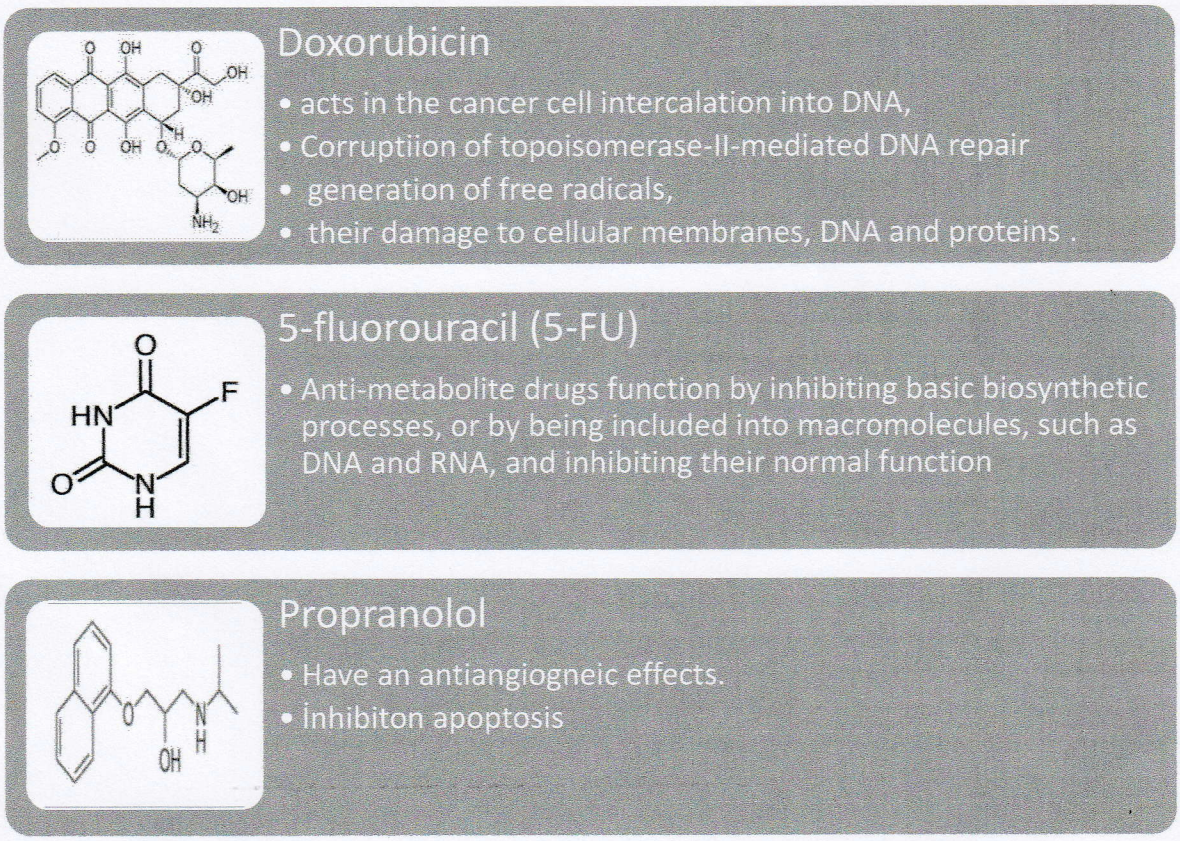

Figure 1: Effect mechanisms of Doxorubucin, 5-FU, Propranolol.

References:

139. Li, Feifei, Changqi Zhao, and Lili Wang. Molecular-targeted agents combination therapy for cancer: Developments and potentials. (2014) ***International Journal of Cancer*** 134.6:1257-1269.

140. Pasquier, Eddy, et al. Propranolol potentiates the anti-angiogenic effects and anti-tumor efficacy of chemotherapy agents: implication in breast cancer treatment. (2011) ***Oncotarget***; 2.10:797-809.

141. Longley, Daniel B., D. Paul Harkin, and Patrick G. Johnston. 5-fluorouracil: mechanisms of action and clinical strategies. (2003) ***Nature Reviews Cancer;*** 3.5:330-338.

142. Thorn, Caroline F., et al. Doxorubicin pathways: pharmacodynamics and adverse effects. (2011) ***Pharmacogenetics and genomics;*** 21.7:440.

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References:

217. http://www.haberturk.com/saglik/haber/677120-kansere-dev-butce

218. Etzioni R, Urban N, Ramsey S, McIntosh M, Schwartz S, Reid B, Radich J, Anderson G, Hartwell L, The case for early detection. (2003) *Nat. Rev. Cancer*; 3(4):243-252.

Zhang G, Fiore G. L, Clair T. L. St, Fraser C. L, Difluoroboron Dibenzoylmethane PCL-PLA Block Copolymers: Matrix Effects on Room Temperature Phosphorescence. (2009) ***Macromolecules***; 42(8):3162-3169

PP – 98 Investigation of Cytotoxic and anti- proliferative effects of Doxorubicin (DOX) and Caffeic Acid Phenethyl Ester (CAPE) on MDA-MB 231 breast cancer cell line

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Background: Breast cancer is one of the leading causes of mortality among women worldwide.Cell viability assays and cytotoxic effect of drugs are important tools in oncological research Doxorubicin (DOX) is an anthracycline antibiotic, which a powerful antitumoral drug and one of the most active agents for treatment of breast cancer. Caffeic Acid Phenethyl Ester (CAPE) is a major active component in propolis and it has been previously identified as a strong antioxidant, anti-inflammatory, antiviral and anticancer molecule.
The aim of this study is explore the cytotoxicity effects and cell proliferation of using single drug and combine of Doxorubicin and Caffeic Acid Phenethyl Ester in MDA-MB 231 breast cancer cell line.

Methods: MDA-MB 231 breast cancer cell line was cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing Fetal Bovine Serum (FBS) 10% (v/v) and penisillin-streptomisin 1% (v/v) and incubated at 37°C in a humidified 5% CO_2 incubator. MTT assay was used to determined the cytotoxic effect range of dosage DOX ,CAPE and combine of DOX+CAPE in MDA-MB 231 breast cancer cells. For cell viability,cells were treatment with IC_{50} value for 24 h and 48 h of incubation.

Results: Only Doxorubicin produced an IC_{50} (concentration resulting in 50% inhibition of control growth) of 30 µM, whereas only CAPE resulted in an IC_{50} of 55µM in the MDA –MB 231cell line. Especially, consentration of combine group10µM for Dox.- 15µM for CAPE; according to control group decreased of cell viability in half. DOX+CAPE combine therapy is more effected than singly therapy of this drug. **DOX and CAPE singly therapy was shown decrease in viable cells at 24 h.Treatment with DOX at 48 hours, decreased effect of DOX on the viable cell and cells gained resistance against to drug.** We found in this study, significant decrease of metabolic activity of the cell line with treatment **CAPE at 24 h and 48 h.**

Conclusions: This results indicated that **cell** viability **decreased** treatment with DOX and CAPE compared to single using DOX and CAPE treatment on MDA-MB 231 breast cancer cell. Treatment with CAPE showed regularly decreased viable cells depend on hours but singly Dox treatment at 24 h was more effective than 48 h.

Keywords: *Breast cancer , Doxorubicin ,CAPE*

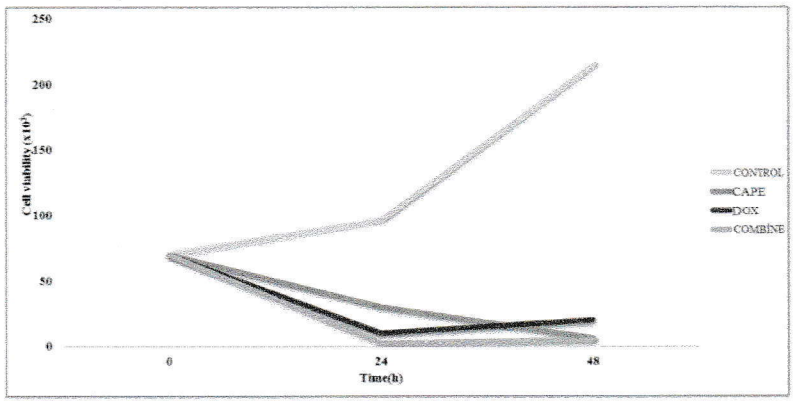

Figure 1: Evaluation of anti-proliferatif effect of DOX (30 µM) ,CAPE (55 µM) and DOX(10µM)+CAPE(15 µM)therapy on MDA-MB 231 breast cancer cell line at 24h and 48h.

References:

219. Anthony SF, Eugene B, Dennis LK. Harrison's Principles of Internal Medicine 16th Ed. New York: The McGraw-Hill Companies,*(2005)* ***Breast Cancer***: 516-23,

220. Bauer K.R., Descriptive Analysis Of Estrogen Receptor (ER)- Negative, Progesterone Receptor (PR)- Negative and HER2-Negative Invasive Breast Cancer, The So-Called Triple Negative Phenotype, (2007)***Cancer,***109(9): 1721-1728