Bio Türkiye

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9 - 11 Eylül 2021

PROGRAM

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9 Eylül 2021, Perşembe (1. Gün) — Salon 1

FARMASÖTİK BİYOTEKNOLOJİ

18.00-18.54 SÖZLÜ BİLDİRİLER - 1 / FARMASÖTİK BİYOTEKNOLOJİ
Oturum Başkanı: Doç. Dr. Gülay Büyükköroğlu *(Anadolu Üniversitesi Farmasötik Biyoteknoloji Anabilim Dalı)*

18.00-18.06 **OP-01:** Construction of Anti-SARS-CoV-2 Phage Displayed Mouse ScFv Library From Hybridoma cells
Kübra Bilgiç, Oya Arı Uyar, Gamze Kılıç, Esin Akçael, Fatıma Yücel, Şaban Tekin, Aylin Özdemir Bahadır, Bertan Koray Balcıoğlu

18.06-18.12 **OP-02:** Genome analysis of a new potential probiotic strain Lactiplantibacillus plantarum DY46 isolated from fermented turnip
Fatih Ortakcı, Ahmet Evren Yetiman, Enes Kotil

18.12-18.18 **OP-03:** Investigation of Protective and/or Therapeutic Effects of Cynara Scolymus Leaf on Diethylnitrosamine-Induced Cognitive Impairment Using Biochemical and Spatial Learning Data
Yesim Yeni, Sidika Genc, Betül Cicek, Mehmet Kuzucu, Ahmet Cetin, Muhammed Sait Ertugrul, Ufuk Okkay, Ahmet Hacimuftuoglu

18.18-18.24 **OP-04:** Development and evaluation of venetoclax and siRNA loaded albumin based carrier systems
Bilgen Çalışkan, Behiye Şenel, Gülay Büyükköroğlu

18.24-18.30 **OP-06:** Investigation of effects of the chitosan/ hyaluronic acid/ honey hydrogels on cell adhesion and proliferation
Ahmet Enes Akdağ, Emine Şalva, Sema Arısoy, Jülide Akbuğa

18.30-18.36 **OP-07:** The Effect of the C60 Nanoparticle on the Expression of Some Apoptotic Proteins in Pancreatic Damaged Rats
Ozlem Gok, Seda Beyaz, Abdullah Aslan, Can Ali Agca, Ibrahım Hanifi Ozercan

18.36-18.42 **OP-08:** Treating Neurotoxicity Developed in Triple Cocultures Created by Transwell Method with Graviole Plant
Sıdıka Genç, Ali Taghizadehghalehjoughi, Yeşim Yeni, Ahmet Hacımüftüoğlu

18.42-18.48 **OP-09:** Evaluation of Anticancer Potential of a Cholesterol Lowering Drug and Its Synthetic Intermediates
Sefayi Merve Özdemir, Esen Bellur Atici, Ali Çağır

18.48-18.54 **OP-10:** Gold Nanoparticles Improve Locomotor Activity Rhythm and Alleviate Oxidative Stress in a Mice Model Nitrosamine–Mediated Degeneration
Sıdıka Genç, Yeşim Yeni, Betül Çiçek, Mehmet Kuzucu, Ahmet Cetin, Kemal Volkan Ozdokur, Ufuk Okkay, Ahmet Hacımüftüoglu

OP-04

DEVELOPMENT AND EVALUATION OF VENETOCLAX AND siRNA LOADED ALBUMIN BASED CARRIER SYSTEMS

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ABSTRACT

Cancer, a worldwide health problem is the result of a tumor formation characterized by uncontrolled cell proliferation. Bcl-2 protein encoded by the Bcl-2 gene plays a significant role in controlling apoptosis and increasing cell survival in response to various apoptotic stimuli. Also the studies on siRNAs that suppress the Bcl-2 gene have increased. The purpose of this study was to determine the physicochemical properties of developed formulas and to overexpress the Bcl-2 gene separately and together (siRNA / ABT) into the albumin nanoparticles, which were used in the clinic to suppress the Bcl-2 gene. Another aim of this study is to investigate the activity of the formulas on breast cancer cells in vitro. As a result, the evaluation of the efficacy of Venetoclax in breast cancer and minimizing its toxic effects by using the delivery system were investigated.

INTRODUCTION

Venetoclax (ABT) blocks an important stimulatory pathway in cell survival in tumor cells where it overexpresses Bcl-2 and leads to cell death. ABT is the first FDA-approved (April 2016) drug that targets the Bcl-2 protein in cancer cells and is used in the treatment of patients with Chronic Lymphocytic Leukemia (CLL). Although its inhibitory properties have been observed in tumor cells in vitro, it has no clinical application outside of CLL (AbbVie Inc., 2016). Drugs that are accepted as primary treatment agents for many types of cancer show serious dose-limiting side effects after a certain period of time. In addition, intrinsic or acquired multidrug resistance is one of the most important problems encountered during treatment. Overexpression of Bcl-2 can also lead to the development of resistance to chemotherapy and radiation for various types of cancer. Recently, the effectiveness of this methodology has been explored in potential therapeutic studies using small silencing RNAs (siRNAs) that regulate downstream gene expression in various models. Combination of two or more therapeutic modalities with different mechanism of action is seen as a promising therapeutic approach in cancer treatment.

In this approach, it is aimed to use anticancer drug and siRNA together, to reduce the toxic effect in the treatment by increasing the target selectivity through albumin carrier systems, to ensure that the drug resistance can be effectively resisted, and thus to increase the therapeutic efficacy synergistically.

Three different albumin-based nanoparticles, ABT loaded, siRNA loaded and ABT/siRNA loaded, were prepared and the effectiveness of these nanoparticles on breast cancer cells in which Bcl-2 overexpressed was investigated.

MATERIALS AND METHODS

The desolvation method is the most widely used method in the synthesis of protein-based nanoparticles using water-miscible organic solvents such as ethanol or acetone. It is based on the principle of denaturing albumin with the help of the addition of ethanol. Its solubility gradually decreases and phase separation occurs. This causes a decrease in the dielectric constant of the mixture an the desolvation of this constant change in phase can determine the size of the formed particles. After the particle size and zeta potentials of the nanoparticles prepared by the desolvation method **(1)** were evaluated and optimized, the genetic material was adsorbed and ABT loaded, siRNA loaded and ABT/siRNA loaded nanoparticles were developed.The cytotoxic effects of the prepared nanoparticle formulations on MDA-MB-231 and NIH-3T3 cell lines were investigated.

RESULTS AND DISCUSSION

As a result of the characterization studies carried out in the developed formulations, F6 was found to be the most stable formulation had the zeta potential of 41.4 ± 0.95 mV, with a particle size of 364.72 ± 7.4 nm. Also, ABT-free (placebo) formulation F5 with a 28.6 ± 0.36 mV, 193.38 ± 3.8 nm was selected (Table 1).The amount of genetic

material that can be loaded into the F5 and F6 formulations was determined (Figure 1).

As a result of the evaluation of the cytotoxic effect in cell culture studies, it was observed that the F6_siRNA formulation had more toxic effects on cancer cells, and the cell viability decreased to 38% in the first 24 hours in the presence of 15 µg/ml ABT. While no toxic effect of F5_siRNA was observed at 24 hours in breast cancer cell line, it was observed that cell viability decreased to 89% and 75% **(2)**.

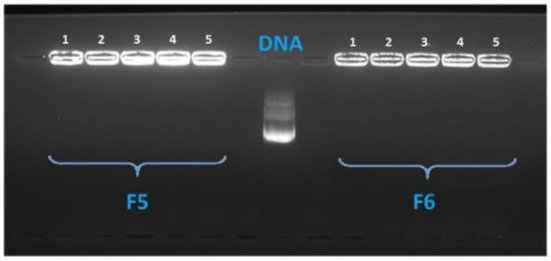

Figure 1. Gel images of F5 and F6 formulations loaded with DNA

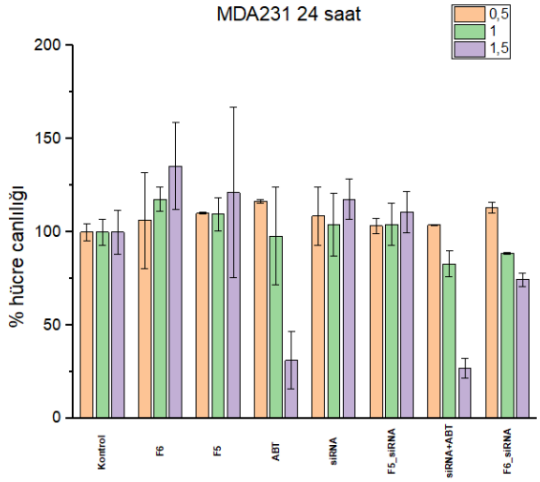

Figure 2. Cytotoxic effect evaluated in MDA-MB 231 cells after 24 hours

Table 1. Comparison of the contents and codes of the formulations with particle size, PDI and zeta potential values

	ABT 1992 mg	%0.04 Chitosan 500 µL	%4 Tween 80 1 mL	pH	Particle size (nm)	PDI	Zetapotential (mV)
Alb F	-	-	-	7,4	50 ±2,4	0,102 ±0,01	6,17±0,65
F1	+	-	-	7,4	1360 ±54,7	0,562 ±0,05	16,21±0,57
F2	+	-	+	7,4	140,41 ± 4,5	0,229 ±0,01	-26,51±0,86
F3	+	-	-	5,9	547,40 ± 8	0,569 ±0,05	8,91± 0,23
F4	+	+	-	5,98	581,43± 37,2	0,368 ±0,03	46,90± 073
F5	-	+	-	7,4	193,38 ± 3,8	0,273 ±0,01	28,6 ± 0,36
F6	+	+	-	7,4	364,72 ±7,4	0,253 ±0,05	41,4 ± 0,95

CONCLUSION

When the cytotoxicity of the formulations was evaluated, the higher efficacy of siRNA in MDA-MB-231 cells suggested that the designed nanoparticles could specifically affect the cancer cell.

It is an expected situation that no significant toxicity will be observed on cells due to effects such as the restrictions on the uptake of negatively charged and unstable naked siRNA and its endosomal degradation. However, as a result of studies conducted in this area, it has been determined that naked siRNA can affect cellular pathways without being fragmented in intracellular traffic, and may have a slightly toxic effect (3, 4, 5, 6).

With this study, it has been scientifically shown that albumin-based carriers contribute to the field of gene transfer. With the synergistic effect of ABT and Bcl-2 siRNA, its therapeutic efficacy has increased and it has been shown that it is possible to reduce dose-dependent toxicity by silencing Bcl-2 protein **(7).** The efficacy of ABT, which is used in the treatment of chronic lymphocytic leukemia (CLL) in the clinic, in breast cancer cells has been investigated for the first time and the results are promising for future studies.

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DOÇ. DR. GÜLAY BÜYÜKKÖROĞLU

9-11 Eylül 2021 tarihlerinde çevrimiçi olarak düzenlenen
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