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Fund “Nauka” Project № 23011 Resume – Competition-Based Session 2023:

“Conventional 2D and modern 3D ALI cell culture models for studying the antimicrobial and cytotoxic properties of new therapeutic agents and nano-structured drug carriers”

Project leader: Chief assist. prof. Nadezhda Antonova Ivanova, PhD

This project aims to study the therapeutic and cytotoxic potential of drug-carrying nanoparticles by means of investigations on 2D and 3D cell cultures. The subject of the research are nanostructured lipid carriers, metal (silver) nanoparticles, and vesicular nanosystems – all obtained and characterized or under development in the Faculty of Pharmacy, Medical University of Varna. A pilot antimicrobial screening of the chosen drug-loaded and non-drug-loaded nanostructures will be carried out against common pathogens – *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Candida albicans, Lactobacillus casei, Streptococcus mutans, Staphylococcus epidermidis*. The particles’ pharmaco-technological parameters will be adjusted and optimized with regard to the future therapeutic goals. The antiviral activity and cytotoxicity of the test models will be initially assessed on conventional 2D cell cultures. The best-performing samples showing a broad antimicrobial spectrum of activity along with a low to absent toxicity will be subjected to further *in vitro* studies on 3D air-liquid interface (ALI) cell models. The latter allow precise *in vitro* evaluation, comparable with the *in vivo* studies’ reliability. In the scope of this project, ALI-differentiation of primary human basal cells and keratinocytes in 3D models of bronchial ciliated respiratory epithelium and skin will be carried out. The cytotoxicity and antiviral potential of the test samples will be thoroughly investigated upon experimental infection with Influenza type A (strains H3N2 and H1N1), Coronavirus OC43, and/or Herpes virus 1 (HSV-1). The project team hopes to gain experience and knowledge in innovative 3D cell models and make a significant contribution to the development of this research field at the Medical University of Varna.

Expected results:

1. Obtaining reliable data regarding the antiviral activity and cytotoxicity of the selected drug nano-carriers from *in vitro* tests on 3D ALI cultures;
2. Obtaining information about the interference of the nanoparticles with the microbiome;
3. Obtaining information about the antibacterial and antifungal potential of the drug-loaded nanostructures;
4. Ensuring the prospect for selection of a broad-spectrum antimicrobial therapeutic combination with low toxicity with a view to inclusion in a pharmaceutical dosage form and development of a medicinal product or medical device;

5. Publication of the results: 2 articles in refereed and indexed journals with impact factor (IF) and 2 articles in Scripta Scientifica Pharmaceutica.