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Fund “Nauka” Project № 23009 Resume – Competition-Based Session 2023:

“Design, preparation and study of isatin hybrid molecules with putative broad-spectrum antimicrobial activity and potential application in implantology”

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Implantology has undergone significant progress over the past few years with the introduction of implants into clinical practice. Despite the therapeutic success of this part of medicine, the risk of postoperative infections continues to be a danger to the health of patients and requires the development of new antimicrobial agents. The design of new molecules with antibacterial activity is imperative due to increasing antimicrobial resistance. New compounds should overcome the limitations of current drugs and offer alternatives to combat a wide range of pathogens, including multidrug-resistant ones. The interest in the design of hybrid molecules, in order to obtain compounds with improved biological activity, has grown significantly in the last two decades. The aim of the current project is the design and synthesis of chemically diverse hybrid derivatives of isatin with potential broad-spectrum antibacterial activity, allowing their use in implantology for the prevention and treatment of post-operative infections. The main tasks of the project include the synthesis, characterization and evaluation of the antimicrobial activity in vitro, in silico and ex vivo of a series of new hybrid isatin molecules intended for use as antimicrobial agents. The methods used in the project include basic chemical approaches in organic synthesis, liquid chromatographic and spectral instrumental methods for characterizing chemical molecules and extensive protocol tests in artificial conditions, including computer simulations, to prove the activity and structure-activity relationship of the newly synthesized compounds. Finally yet importantly, well-established microbiological tests will be applied to prove the potential anti-infective activity of the newly synthesized compounds, using reference strains and clinical isolates from the oral cavity. Expected results include the preparation and validation of molecules with potential antimicrobial properties. This will contribute to a better understanding of their efficacy and biological activity, as well as their potential in combating implantology-related infections. The subsequent implementation of these innovative isatin-based molecules in clinical practices may provide a significant improvement in the prevention and treatment of infections associated with medical implants, providing solutions that are more effective for patients.

Conducting targeted synthesis of new anti-infectives including isatin-based oneswith potential application in implantology may have the following expected results:

1. Successful synthesis of diverse hybrid molecules derived from isatin;
2. Extensive structural characterization of the newly synthesized molecules, clarifying their chemical properties and functional groups;

3. Establishing the structure-activity relationship of the new hybrid isatin molecules and elucidating their mechanism of action through computer simulations and molecular docking, which will optimize molecular design;
4. Establishing the potential broad-spectrum action of the newly synthesized molecules against pathogens associated with postoperative infections could improve the protection against bacterial infections after surgical interventions or implantations, which would reduce the risk of infections after such procedures. It would also extend the life of the implants, reduce the likelihood of their rejection by the body and reduce the need for additional medical procedures, which could lead to savings in healthcare costs;
5. Identification of minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) for the newly synthesized compounds will demonstrate their effectiveness in inhibiting microbial growth;
6. Evaluation of synergistic effects, if any, among hybrid molecules will provide valuable information on their combined antimicrobial efficacy;
7. The statistical analysis of the collected data will contribute to the complex understanding of the significance and implications of the study in the context of implantology and antimicrobial therapy.