3,3'-Bisindolylmethane Derivatives as Antibiotic Resistance Disruptors

Victoria Lipson^{a,b*}, Mikola Lyapunov^a, Olena Bezugla^a, Anna Lyapunova^a, Igor Zinchenko^a, Volodymir Vakula^a, Svitlana Dzhoraieva^c

^aInstitute of Functional Materials Chemistry SSI "Institute for Single Crystals" of NAS of Ukraine, 60 Nauky Ave., Kharkiv 61072, Ukraine

^bChemistry School, V.N.Karazin Kharkiv National University, 4 Svobody Sq., Kharkiv 61022, Ukraine

°SE "Institute of dermatology and venerology of NAMS of Ukraine", Chernyshevska Str., 7/9, Kharkiv 61057, Ukraine

* Corresponding author: lipson@ukr.net

The presenting author: Victoria Lipson

Abstract

Resistance to antibacterial drugs and the emergence of multi-resistant strains of microorganisms is a problem of global importance that require a rapid response from a wide range of researchers [www.who.int/health-topics/antimicrobial-resistance]. The proposed report examines the current trends in the search for antibacterial agents. Particular attention is paid to the opportunities opened up by the combined use of substances of both natural and synthetic origin that do not have antibiotic properties, but in combination with known drugs can significantly increase their effectiveness in the fight against multi-resistant strains of pathogens. Our own results on the synthesis of such substances, in particular new derivatives of 3,3'-bisindolylmethane (BIM), as potential components of drugs capable of increasing the effectiveness of representatives of various classes of antibiotics in the fight against bacteria of the ESKAPE group (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, Enterobacter spp.) - the main cause of nosocomial infections and increased mortality - are presented. The results of microbiological screening of the obtained compounds on standard and clinical strains of the indicated microorganisms, as well as Escherichia coli and Candida albicans fungi are presented. Pharmaceutical compositions are proposed, which include an active pharmaceutical ingredient with antibacterial properties, a certain BIM and excipients. The effect of these compositions on the biofilm formation of pathogens is determined.

Part of this work was carried out with the financial support of the National Research Foundation of Ukraine, grant No. 2022.01/0087.

Keywords: antibiotic resistance, 3,3'-bisindolylmethanes, pharmaceutical compositions, antibiofilm properties