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Editorial

Special Issue on Synthesis of Novel Heterocyclic Compounds and Evaluation of Their Antimicrobial Activity

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Since their discovery or, to be exact, their definition, the chemistry of heterocyclic compounds has rapidly developed, and the range of their application has grown wider. At present, the vast majority of low-molecular-weight compounds on the market are heterocyclic ones, being mainly nitrogen heterocycles. They have a variety of activities, although the main direction of their use employs their antimicrobial activity against practically all forms of microorganisms. Of course, among them, the compounds of five- and six-membered rings are the most important, which why these compounds have been the most intensively studied for new drug discovery and development.

This Special Issue is intended to collect and present selected recent experimental research data and conceptual works describing new methods for the synthesis of new compounds with heterocyclic structures and methods of proving and quantitatively evaluating the antimicrobial activity of these new chemical entities.

The presented Special Issue collects seven papers (including five experimental works, a conceptual work and a review) concerning various types of heterocyclic compounds and their highly diversified antimicrobial activity. Apostol et al. [1] describe the antimicrobial activity of 28 compounds from 1,3-oxazole and 1,3-oxazol-5-one groups, as well as 21 of their acyclic precursors. All these products have been tested both in silico and in vitro with the use of qualitative and quantitative assays to investigate their antimicrobial potential against planktonic and biofilm-embedded microbial strains. Some of the evaluated new products showed promising antimicrobial and antibiofilm activity that was dependent on the structure of their chemical scaffold and their lipophilic character. Askri et al. [2] describe a three-component cascade reaction leading to the formation of 17 new spiropyrrolidine derivatives in an efficient and convenient way under mild conditions. The structures and full stereochemistry of the obtained products were determined using spectral methods, and a representative compound was subjected to a single-crystal X-ray diffraction analysis. The antifungal and antibacterial activities of these compounds were a little weaker than those derived using amphotericin and tetracycline as reference substances. Moreover, the compound showing the highest activity was docked into the binding sites of glucosamine 6-phosphate synthase and methionyl-tRNA-synthase. The above products also showed acceptable predictive ADMET properties and good drug ability. In the next paper, Potapov et al. [3] report the synthesis of a group of new and highly soluble compounds as a product of annulation reactions of 8-quinolinesulfenyl halides with natural origin alkenes. Using this method, a series of [1,4] thiazino[2,3,4-*ij*]quinolin-4-ium was obtained with almost quantitative yields. Reactions with styrene derivatives and other terminal alkenes proceeded in a regioselective manner but with the opposite regiochemistry. In this case, styrene showed greater reactivity than the other terminal alkenes. The compounds synthesized in this way were tested for their activity against bacteria of the genera *Enterococcus*, *Bacillus* and *Escherichia*. Some of the tested substances showed a significant activity relative to that of gentamicin. The reaction products of 8-quinolinesulfenyl halides with 1H-indene, eugenol, methyl eugenol and 1-heptene proved to be particularly effective. Lijewski et al. [4] described the synthesis

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of complex compounds with condensed heterocyclic rings, which contained a porphyrazine system fused with pyrazine rings, which were substituted with a menthol–thiophenyl group in the peripheral zone. Moreover, inside the porphyrazine ring, there was a magnesium ion (Mg(II)) centrally bonded through coordinated bonds as a complex connection. All intermediate and final compounds obtained were thoroughly spectrally characterized using the 2D NMR technique. Their photochemical stability was also determined, confirming the high resistance of the macrocyclic system to visible light, which may also be important for their biological activity, including antimicrobial activity. Paruch et al. [5] report in their work the synthesis of 15 new 4-methyl-1,2,3-thiadiazole-5-carboxyhydrazide derivatives substituted with various substituents in the hydrazine moiety. The most active of the obtained products turned out to be the one with an additional heterocyclic substituent in the form of a 5-nitro-2-furoyl group. All obtained compounds that are derivatives of thiazolidines were tested for their activity towards bacteria strains with high antibiotic resistance, which is nowadays one of the most serious therapeutic problems. In the next work, Catalano et al. [6] reviewed progress in the preparation of metal complexes with Schiff bases, which were used, among others, as anti-proliferative agents for various purposes. The heterocyclic system in the compounds described here is present within the rings that are the ligands in these products or formed as a result of cyclization with the participation of a linearly bonded nitrogen atom to the appropriate complex connection, which leads to chemical entities similar to classical heterocyclic compounds. This review article cited data for 48 types of compounds known from the previous, scattered literature information on this topic. The earlier mentioned pyrazine system also appeared in the concept paper of Cherniienko et al. [7], in which, based on a review of the literature data, an attempt was made to correlate the odor properties and the antibacterial ability of 40 pyrazine derivatives found in cocoa and chocolate and responsible for their specific smells. The antimicrobial properties of these compounds have been calculated for various types of microorganisms using widespread computational prediction programs. As a result, a significant degree of correlation was found between the odor threshold, type and intensity of the aroma of selected pyrazine compounds and their antimicrobial activity. However, the thesis about the potential healing effects of chocolate requires further extensive experimental research.

Although this Special Issue has now been edited, we are fully aware that it does not exhaustively cover the subject. The research work on heterocyclic compounds has continued and surely already brought interesting new results not presented in this Special Issue. It seems to us that derivatives of thiazolidines and trioxanes are particularly promising. The area of their prospective application includes the microbiological threats of great current interest, like fighting viral diseases, especially the epidemic ones caused by coronaviruses, and the eradication of malaria and its source *Plasmodium malariae*. We hope that science will satisfy social expectations in this area.

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