This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No 101035813

New lidocaine derivatives showing antimicrobial activity as new APIs with low environmental impact

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Currently, the most popular anesthetic drug is lidocaine – synthetic chemical compound from the amide group. Unfortunately, due to its short duration of action of only a few hours, it requires repeated administration during longer treatments. For this reason, scientists are looking for new compounds with long-lasting action. Exploring the properties of lidocaine by derivatizing it and combining it with a 2-furoic anion, which exhibits bactericidal activity, could lead to formation of new multifunctional active pharmaceutical ingredients (APIs). The aim of the study was to synthesize novel APIs consisting of bromide or 2-furoic anion and cation representing quaternary lidocaine derivatives containing 2 and 14 carbon atoms in the alkyl chain. It was planned to determine their antimicrobial activity and ecotoxicological profile.

The desired compounds were obtained *via* quaternization of lidocaine with appropriate alkyl halide and subsequent ion exchange reaction. The structures of the products were confirmed by spectroscopic techniques and the water content was measured according to the Karl Fisher method. MIC and MBC parameters were determined against *Staphylococcus aureus*. Eventually, the ecotoxicological profile was assessed towards *Artemia franciscana* and *Chlorella vulgaris* and analyzed in accordance to the Global Harmonized System (GHS). Spectral analysis confirmed the purity of the substances, and studies of physicochemical properties showed an increase in hydrophobicity with alkyl chain elongation. *N*-tetradecyllidocaine, was classified into category I acute aquatic toxicity towards green algae, while in the case of impact on *A. fransicana* it was assigned into II acute aquatic toxicity. Interestingly, *N*-ethyllidocaine turned out to be safe to all of the aquatic organisms. The presence of the 2-furoic anion does not increase the compounds' toxicity in any case. The obtained APIs proved to be effective inhibitors of *S. aureus* growth.

The studies conducted demonstrate the importance of investigating not only the pharmacological properties of new pharmaceuticals, but also their potential long-term impact on the environment. The performed research revealed high application potential of the newly obtained lidocaine derivatives. Products' low environmental impact combined with simultaneous favorable antimicrobial and anesthetic properties will allow them to be implemented as an active ingredients in ointments and emulsions.

This research was funded by the Ministry of Education and Science in Poland as a subsidy to Poznan University of Technology, Poland (0912/SBAD/2408).