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"Design and synthesis of peptide conjugates with potential antimicrobial activity"

For nearly 80 years, antibiotics have been widely used to treat many types of infections [1]. Their overuse and misuse have resulted in the presence and spread of microbial drug resistance worldwide. This is one of the greatest public health threats, with approximately 33,000 deaths per year in Europe caused by antibiotic-resistant strains. It is estimated that if the rate of spread of drug-resistant microorganisms in the countries of the European Union and the European Economic Area remains at the same level, the costs associated with the treatment of diseases caused by them will reach more than 1 billion euros per year [2]. This emphasizes the need to search for alternative treatments that are effective against a broad spectrum of microorganisms. One of the most promising directions of this search is the conjugation of a chemotherapeutic agent with a carrier, resulting in molecules with new and unique properties compared to their constituent compounds.

By conjugation, it becomes possible to introduce, into the cell, hydrophilic therapeutic agents and also improves their pharmacokinetic properties. The final properties of the conjugate are influenced not only by the drug molecule but also by the peptide and linker used, which can be cleaved inside the pathogen.

The main aim of my dissertation was to design, develop synthesis methods and synthesize fluoroquinolone conjugates with potential antimicrobial activity. I used peptides with antimicrobial (AMP) and/or cell-penetrating (CPP) properties as carriers. I have linked chemotherapeutics to peptides directly or indirectly using different types of linkers.

In this dissertation, I designed and synthesized 16 novel peptide conjugates with ciprofloxacin or levofloxacin, which showed antimicrobial properties. The obtained bioassay results showed a significant effect of the linker type on antimicrobial activity and the possibility

of expanding the spectrum of the chemotherapeutic agent by its conjugation with the CPP peptides.

[1] Hutchings M, Truman A, Wilkinson B, *Antibiotics: past, present and future,* Curr. Opin. Microbio, 2019, 51, 72–80

[2] Organizacja Współpracy Gospodarczej i Rozwoju (2019). *Antimicrobial Resistance Tackling the Burden in the European Union.*