ENZYME-DEGRADABLE POLYION COMPLEX FOR ANTIMICROIBAL DELIVERY

Sameh El Sayed [1], Francisco Fernandez-Trillo[1]

[1]School of chemistry, University of Birmingham, B15 2TT Birmingham, UK

Background: Antibiotic resistance microbes will cause 10 million death by 2050 according to the WHO, more than all cancers if no effective treatment found. There are several efforts need by governments and industry to look for new antimicrobial agents. One direction of research is relay on the new formulation of the last few antibiotics that still toxic against pathogenic bacteria may be a good solution faster than looking for new antibiotics. This including the delivery of these antibiotics inside the degradable bacterium enzymes selectively in the site of infections.

Methods: Here, we describe the preparation of novel polyion complex (PIC) particles for the delivery of Polymyxin B (*Pol-B*), an antimicrobial peptide currently used in the clinic as a last resort antibiotic against multidrug-resistant gram-negative bacteria *Pseudomonas aeruginosa*. Towards this end, we have prepared polymer containing peptide sequence (-Glu-Gly-Leu-Ala-) this sequence is selectively degraded by *pseudolysin,* an elastase produced by this pathogenic bacterium.

Results: A range of conditions for the controlled assembly of Pol-B with polymer containing peptides has been identified that result on stable colloidal PIC particles containing different Pol-B:Polymer ratios with size around 120 nm. The prepared nanoparticles showed significant stability under simulated physiological conditions such pH, osmotic pressure, and temperature. Furthermore, preliminary evaluation of the antimicrobial activity of these Pol-B containing PIC particles has been performed, by monitoring their effect on the growth of *Pseudomonas aeruginosa.* The prepared PIC showed very low toxicity to the mutant bacteria that does not produce *pseudolysin* enzyme in the infection site while undergo high degradation rate (80% in 4h) with antibiotic release in the presence of the wild type. In addition to high stability against the Human elastase enzyme that often found in the infection site, this proves the high selectivity of these nanoparticles toward the drug delivery in the presence of specific target.

Conclusions: Bacterial enzyme degradable nanoparticles were prepared and used for the selective fast delivery of antibiotic in the infection site caused by a multidrug-resistant gram-negative bacteria *Pseudomonas aeruginosa.* The presented nanoparticles showed significant stability in biological conditions and high selectivity as well as fast delivery. These polyplex formulation method has promising potential for antimicrobial delivery as it's easy to prepare, present stability, selectivity, and lead to the release of the drug with complete efficiency.