

Poster presentation

Anti-bacterial activity of poly-L-lysine conjugates

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Since 15 years, our research group works on a new therapeutic approach of chronic diseases [1,2], we present here new drug candidates able to fight against GRAM – bacteria and some multi-resistant ones. These drugs based on the synthesis of iatrogenic polypeptides on which are linked endogenous small sized molecules. The different bacterial strains used in this study were: GRAM – strains: *Citrobacter koseri*, *Citrobacter diversus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Morganella morganii*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Alcalescens dispar*, and *Hafnia alvei*; and antibiotic multi-resistant Gram – strains: *Escherichia coli*, *Pseudomonas aeruginosa* and *Alcalescens dispar*.

Before testing, we have produced many fatty acid poly-L-lysine conjugates. Fatty acids and small compounds linked to PL were: acetic acid (C₂)-PL, lactic acid (C₃)-PL, propionic acid (C₃)-PL, pyruvic acid (C₃)-PL, butyric acid (C₄)-PL, Succinic acid (C₄)-PL, glutaric acid (C₅)-PL, caproic acid (C₆)-PL, caprylic acid (C₈)-PL, azelaic acid (C₉)-PL, capric acid (C₁₀)-PL, lauric acid (C₁₂)-PL, myristic acid (C₁₄)-PL, palmitic acid (C₁₆)-PL, Oleic acid (C₁₈)-PL. Each conjugate was evaluated on the different bacteria strains.

On the Petri dish test, the densitometric criteria of bacteria were always a value of 0.5 in the McFarland scale. The evaluation of the inhibition has been done for each PL-conjugates tested on each bacterial strain. Thus, the solutions were considered as bactericidal when after incuba-

tion in the optimal conditions no colonies appears to grown in period of 24 hours or more.

First of all, we have found that: 1) the most active compounds were: C₄-PL, C₈-PL, C₁₀-PL, C₁₂-PL; 2) the major part of bacteria strains were sensitive. To increase the bactericidal effect of fatty acid-PL conjugate, we have combined different mixtures and found that the best was: C₁₀-PL-C₁₂ and C₄-PL. This mixture was also tested on antibiotic multi-resistant gram – strains. The strongly bactericidal activity was obtained after: 1) 3 hours for *Escherichia coli*; 2) 5 hours for *Pseudomonas aeruginosa*.

These new drug candidates were effective on GRAM – bacteria inhibiting completely their development. The effects were independent of the cell wall. Our data show: 1) the importance of the fatty acid when they are linked to PL; 2) the efficacy of different products (bactericidal activities) on strains which were in some cases multi-resistant. These conjugates open new therapeutic perspectives for chronic diseases in which bacteria are implicated.

References

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