BMC Proceedings

Poster presentation

Anti-bacterial activity of poly-L-lysine conjugates

Michel Geffard*[1,2,3], Jean François Peroteau[2], Sébastien Duleu[2] and Marie Pierre Dabadie[1]

Address: [1]GEMAC, Saint Jean d'Illac, 33127, France, [2]IDRPHT, Talence, 33400, France and [3]IMS-ENSCPB, Pessac, 33600, France

Email: Michel Geffard* - mg.idrpht@wanadoo.fr

* Corresponding author

from Infectious diseases of the nervous system: pathogenesis and worldwide impact
Paris, France. 10–13 September 2008

Published: 23 September 2008

BMC Proceedings 2008, **2**(Suppl 1):P22

This abstract is available from: http://www.biomedcentral.com/1753-6561/2/S1/P22

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 *Alkalescens dispar*.

Before testing, we have produced many fatty acid poly-L-lysine conjugates. Fatty acids and small compounds linked to PL were: acetic acid (C_2)-PL, lactic acid (C_3)-PL, propionic acid (C_3)-PL, pyruvic acid (C_3)-PL, butyric acid (C_4)-PL, Succinic acid (C_4)-PL, glutaric acid (C_5)-PL, caproic acid (C_6)-PL, caprylic acid (C8)-PL, azelaic acid (C_9)-PL, capric acid (C_{10})-PL, lauric acid (C_{12})-PL, myristic acid (C_{14})-PL, palmitic acid (C_{16})-PL, Oleic acid (C_{18})-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 incubation 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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