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(71) Applicant (for all designated States except US): **NORTHERN ANTIBIOTICS OY** [FI/FI]; Eskolantie 1, FI-00720 Helsinki (FI).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **VAARA, Martti** [FI/FI]; Aino Ackténtie 10 A 7, FI-00400 Helsinki (FI). **VAARA, Timo** [FI/FI]; Itäinen Puistotie 16 C 14, FI-00140 Helsinki (FI).

(74) Agent: **KOLSTER OY AB**; Iso Roobertinkatu 23, P.O. Box 148, FI-00121 Helsinki (FI).

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(54) Title: POLYMYXIN DERIVATIVES AND USES THEREOF

(57) Abstract: The present invention relates to a polymyxin derivative wherein R1, R2 and R3 are optional and R1, R2, R3, R5, R8 and R9 are cationic or neutral amino acid residues selected so that the total number of positive charges at physiological pH is at least two but no more than three; and to a combination product comprising at least two such derivatives. The invention further relates to a method for treating, alleviating or ameliorating an infection in a subject, caused by a Gram-negative bacterium by administering a therapeutically effective amount of a derivative according to the present invention to said subject; to a method for sensitizing Gram-negative bacteria to an antibacterial agent by administering, simultaneously or sequentially in any order a therapeutically effective amount of said antibacterial agent and a derivative according to the present invention to said subject; to methods for developing novel antibiotics; for reducing the nephrotoxicity, for improving the pharmacokinetic properties of natural polymyxins and octapeptides; and for sensitizing clinically important bacteria to a host defence mechanism complement present in serum. Finally, the invention relates to a process for preparing such polymyxin derivatives.



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