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Conjugation of vancomycin with transportan 10 improves the antibiotic's qualities

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This study aimed to investigate whether the conjugation of vancomycin (Van) with transportan-10 (TP10) improves the antibiotic's pharmacodynamics and pharmacokinetics.

The procedures used in this study involved:

1) chemical synthesis of four different conjugates of Van with TP10,

2) determination of MIC for each single compound and the conjugates,

3) qualitative determination of Fl-[Lys7(PEG4-Van)]TP10 in brain slices or quantitative [Lys7(PEG4-Van)]TP10 in brain homogenate after intravenous pre-treatment of mice with an appropriate conjugate,

4) determination of toxicity for Van-PEG3-TP10, Van-PEG4-TP10.

All conjugates showed antibacterial action on clinical MRSA strains, and the most prominent effect was observed after exposition of the 12673 strain with TP10-Ala(PEG4-Van) or [Lys7(PEG4-Van)TP10. The response of Van-resistant Enterococcus spp. to the treatment with the conjugates was rather weak. [Lys7(PEG4-Van)]TP10 coupled with fluorescent dye was visible in the mouse brain slices. Additionally, the amount of the conjugate in the mouse brain homogenate was about 200 times bigger than that of Van. The erythrocyte lysis assay indicated relative safety of the two chosen conjugates. Van in the form of a conjugate with TP10 acquires superior pharmacodynamic (potent antimicrobial action on 12673 MRSA clinical strain) and pharmacokinetic (prominent access to the brain) properties, with no increase in toxicity.

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