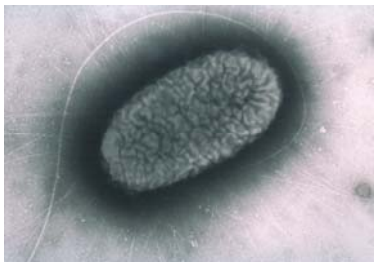

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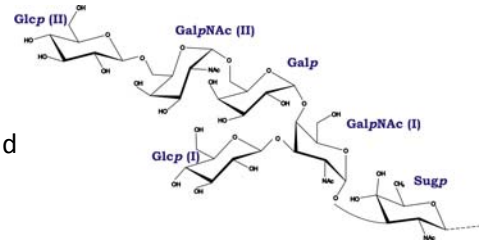

ABSTRACT - POSTER 25

Chemical synthesis of vancomycin derivatives modified with sugar and peptide fragments

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New generation of drugs introduced into therapy against *Staphylococcus aureus* and other Gram-positive bacteria were glycopeptide antibiotics. The most widespread and most commonly used antibiotics were vancomycin and teicoplanin. They were discovered respectively in 1956 and 1978. For many years only these antibiotics were effective in the treatment of infections caused by MRSA strains. This opens a new chapter in the development of medicine and the fight against MRSA. For years, no vancomycin-intermediate resistant *S. aureus* (VISA) or vancomycin-resistant *S. aureus* (VRSA) strains were isolated. The first strains carrying full resistance against vancomycin appeared at the turn of the century.

Understanding the mechanisms of glycopeptide antibiotic action took many years. Pioneers in this area were Perkins and Nieto. In 1969 they discovered that mechanism of action of this antibiotic is leaning on selective binding of vancomycin with peptidoglycan precursor fragment UDP-MurNAc-L-Ala-D-iGlu-L-Lys-D-Ala-D-Ala. Vancomycin creates a stable complex with the terminal fragment of murein (exactly with C-terminal dipeptide fragment D-Ala-D-Ala). Vancomycin inhibits the biosynthesis of peptidoglycan by accumulation of UDP-muramyl-peptide precursors in the cytoplasm.

The replacement of the last D-Ala residue in precursor of peptidoglycan fragment (UDP-MurNAc-L-Ala-D-iGlu-L-Lys-D-Ala-D-Ala) to D-Lac or D-Ser decreases the vancomycin activity about 1000-fold.[1,2,3)] The frequency of resistance to glycopeptide antibiotics has increased significantly over the past decade. Considerable efforts have been made to obtain new semi-synthetic glycopeptides with improved pharmacological properties and activity against resistant strains. The design of new drugs and methods for their study is based on knowledge of the mechanism of action of existing antibiotics.[4)]

There are already many different types of vancomycin modifications aimed at improving its activity. In our work we try to modify the amino group of fragment heptapeptide of vancomycin by joining its sugar and peptide fragments. The introduction of its unit structure characteristic of the bacteria can make that it will interact strongly with parts necessary for the growth inhibition of peptidoglycan.

Acknowledgements: Publication part-financed by the European Union within the European Regional Development Fund

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