View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Archivio istituzionale della ricerca - Università di Palermo

ANTI-STAPHYLOCOCCAL BIOFILM ACTIVITY OF NOVEL SORTASE A (SRTA) INHIBITORS

D. Schillaci[1], M.G. Cusimano[1], A. Leonchiks[2], D. Zhulenkovs[2]

[1]Università degli Studi di Palermo, Palermo, Italy, [2]Latvian Biomedical Research and Study Centre, Riga, Latvia

Pathogenic staphylococci have an extraordinary ability to form biofilms. This characteristic is likely the most important virulence factor of staphylococci in the development of the chronic form of infectious diseases and in biomaterial associated infections (BAI). Staphylococcal biofilms are particularly dangerous because they are more resistant to host immune defence system and have a significantly increased tolerance to conventional antibiotics. There is undoubtedly an urgent need for novel treatments, strategies and anti-staphylococcal biofilm agents.

The Sortase A (SrtA) transpeptidase is responsible for covalent anchoring to the cell wall of various surface proteins (FnbpA, FnbpB, ClfA, ClfB, Protein A, etc.) that have a direct role in the pathogenesis and in the first stage of biofilm formation and because of this it can be considered a good target candidate to design agents that could interfere with virulence mechanism including biofilm formation.

With the aim to discover new SrtA inhibitors, a library of 50000 low-molecular weight compounds was screened in a high throughput assay by using the standard Dabcyl-QALPETGEE-Edans fluorescence resonance energy transfer (FRET)-peptide substrate for measurement of enzyme activity. A group of the selected 38 most potent compounds and 3 known reference inhibitors were further evaluated in an *in vitro* biofilm formation assay at a screening concentration of 10µg/ml using three reference staphylococcal strains *S.aureus* 29213, 6538 and *S.epidermidis* RP62A.

An interesting correlation between inhibition of SrtA and biofilm formation inhibition was observed in many cases especially at a concentration equal or more than IC_{50} determined as SrtA inhibitors.