Two novel synthetic peptoids exhibit rapid in vitro killing of methicillin-resistant Staphylococcus pseudintermedius

Damborg, Peter Panduro; Hansen, Paul Robert; Guardabassi, Luca

Publication date:
2011

Document version
Peer reviewed version

Citation for published version (APA):
Two novel synthetic peptoids exhibit rapid \textit{in vitro} killing of methicillin-resistant \textit{Staphylococcus pseudintermedius}

Peter Damborg\textsuperscript{1}, P. R. Hansen\textsuperscript{2} & L. Guardabassi\textsuperscript{1}

Department of Veterinary Disease Biology (1) and Department of Basic Sciences and Environment (2), Faculty of Life Sciences, University of Copenhagen, 1870 Frederiksberg, Denmark.

Objective

\textbullet\ To assess the \textit{in vitro} efficacy of two newly developed peptoids against MRSP and methicillin-susceptible \textit{S. pseudintermedius} isolates of canine origin

\section*{Introduction}

\begin{itemize}
  \item Methicillin-resistant \textit{S. pseudintermedius} (MRSP) are of increasing concern due to its recent spread amongst dog populations worldwide (Perreten et al., 2010).
  
  \item Limited treatment options are available for MRSP, thus alternative treatment is required to combat these multidrug-resistant microorganisms in the future.
  
  \item Peptoids are oligomers of N-substituted glycines and may mimic biologically active peptides by showing antimicrobial properties.
  
  \item Peptoids resemble peptides except that the side chains are appended to the nitrogen atom of the backbone rather than to the α-carbons. They are also characterised by being more stable \textit{in vitro} towards heat, salt, pH fluctuations and organic solvents compared to peptides. \textit{In vivo}, peptoids are stable to proteolysis whereas peptides are rapidly degraded.
\end{itemize}

\section*{Results}

\textbf{MIC determinations} (Fig. 1)

\textbullet\ Low MICs ranging from 1.56–6.25 µM were observed for B1 and D2. MICs did not differ between MSSP and MRSP.

\textbullet\ MICs were normally distributed – no obvious evidence of resistance in the 50 isolates tested.

\textbf{Time kill kinetics} (Fig 2a and 2b)

\textbullet\ Both B1 and D2 had a concentration-dependant antimicrobial effect on \textit{S. pseudintermedius}.

\textbullet\ B1 acted more rapidly with complete killing at 4 * MIC in 30 min.

\textbullet\ D2 was slightly slower taking 2 hours to kill at 4 * MIC.

\section*{Conclusions}

\textbullet\ Two novel peptoid compounds were shown to have a rapid concentration-dependant effect against \textit{S. pseudintermedius} of canine origin, irrespective of antibiotic resistance phenotypes.

\textbullet\ The rapid killing resembles the pharmacodynamics of antiseptics but the mechanism of action is unknown.

\textbullet\ The next step will be to test the effect and toxicity of topical formulations of the two compounds \textit{in vivo}, for example in a mice skin infection model.

\section*{References}


Acknowledgements

The study is funded by the Danish Centre for Antibiotic Research and Development (DanCARD). The centre is an interdisciplinary collaboration between 11 Danish research groups with the main objectives to develop new antibiotics and increase the efficacy of existing antibiotics (www.dancardproject.dk).