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Two novel synthetic peptoids exhibit rapid \textit{in vitro} killing of methicillin-resistant \textit{Staphylococcus pseudintermedius}

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\section*{Introduction}

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

\section*{Objective}

- 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*{Materials and Methods}

- Prior to the study, 10 newly developed peptoids were tested for their \textit{in vitro} efficacy and hemolysis against various bacterial species. A lysine peptoid hybrid (B1) and a pure peptoid (D2) showing both a low minimum inhibitory concentration (MIC) and a low rate of hemolysis against \textit{S. pseudintermedius} were selected for this study.
- MIC determinations (Fig. 1)
  - Low MIC’s ranging from 1.56-6.25 \(\mu\text{M}\) were observed for B1 and D2. MICs did not differ between MSSP and MRSP.
  - MICs were normally distributed – no obvious evidence of resistance in the 50 isolates tested.

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

- Both B1 and D2 had a concentration-dependent antimicrobial effect on \textit{S. pseudintermedius}.
- B1 acted more rapidly with complete killing at 4 * MIC in 30 min.
- D2 was slightly slower taking 2 hours to kill at 4 * MIC.

\section*{Results}

\textbf{Fig 1. MIC distributions}

- Survival of a standard inoculum (5*10\(^5\)) of this isolate was observed over time after inoculation without peptoid, at 1*MIC and at 4*MIC.

\section*{Conclusions}

- Two novel peptoid compounds were shown to have a rapid concentration-dependent effect against \textit{S. pseudintermedius} of canine origin, irrespective of antibiotic resistance phenotypes.
- The rapid killing resembles the pharmacodynamics of antiseptics but the mechanism of action is unknown.
- 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}


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