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

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

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**Objective**
- To assess the *in vitro* efficacy of two newly developed peptoids against MRSP and methicillin-susceptible *S. pseudintermedius* isolates of canine origin.

**Materials and Methods**
- Prior to the study, 10 newly developed peptoids were tested for their *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 *S. pseudintermedius* were selected for this study.
- B1 and D2 were tested for their *in vitro* activity against 50 clinical *S. pseudintermedius* isolates of canine origin using the broth microdilution method (CLSI, 2008). Ten of these isolates were MRSP and 40 isolates were MSSP, and all isolates had been collected at our diagnostic lab between 2007 and 2010.
- B1 and B2 were also tested in a time kill kinetic study against one representative *S. pseudintermedius* isolate. Survival of a standard inoculum (5 × 10⁶) of this isolate was observed over time after inoculation without peptoid, at 1*MIC* and at 4*MIC*.

**Results**

**MIC determinations** (Fig 1)
- Low MIC’s ranging from 1.56-6.25 µM 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.

**Time kill kinetics** (Fig 2a and 2b)
- Both B1 and D2 had a concentration-dependant antimicrobial effect on *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*.

**Conclusions**
- Two novel peptoid compounds were shown to have a rapid concentration-dependant effect against *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 *in vivo*, for example in a mice skin infection model.

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**References**
