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Abstract

Broad-Spectrum Activity of Antimicrobial Peptoids †

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Abstract: Antimicrobial peptides (AMPs) are naturally occurring host defense molecules, representing an evolutionarily ancient, innate immune mechanism against pathogenic infection. As such, many of these predominantly cationic and amphipathic peptides have been examined for their potential as anti-infective agents. AMP families such as the defensins and cathelicidins exhibit broad-spectrum antimicrobial activity against a wide variety of bacteria, fungi and viruses, initially and predominantly by disruption of the microbial membrane. Due to this physical mechanism, development of resistance by the pathogen is rare. Thus, they represent a great potential for a new type of anti-infective agent. However, due to a variety of reasons, including protease sensitivity and poor bioavailability, they have not been developed into actual therapeutics. To circumvent these issues, we have examined the potential for small molecule mimetics of AMPs, which would be protease-resistant and have better bioavailability. We previously demonstrated the activity of one such class of mimetics, sequence-specific *N*-substituted glycine oligomers, or peptoids, against the human viral pathogen Herpes Simplex Virus-1 (HSV-1), as well as some bacteria. Here, we compare the activity, both in vitro and in vivo, of select peptoids against bacteria, fungi and viruses, to begin to study the structure/activity relationship with a broad spectrum of microbial pathogens. Our results show that some peptoid structures are more active against one type of pathogen than another. However, at least two of the tested peptoids exhibit potent activity against Gram positive bacteria, Gram negative bacteria, fungi and viruses. Our results suggest that these molecules can be developed into potent broad-spectrum antimicrobial agents.

Keywords: Antibiotics; antivirals; antifungals; peptide mimetics

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