

ANTIMICROBIAL ACTIVITY OF CHLORINATED AMINO ACIDS AND PEPTIDESMelanie Coker¹¹*Christchurch School of Medicine and Health Sciences, University of Otago*

When neutrophils phagocytose bacteria they generate the cytotoxic agent hypochlorous acid (HOCl). The specific role HOCl plays in bacterial killing is unclear. In the phagosome HOCl should react primarily with neutrophil proteins to form protein chloramines. This reaction may prevent HOCl from killing the ingested bacteria. Alternatively, chloramines on proteins may have bactericidal activity because they will retain some of the oxidizing potential of HOCl. Therefore, we investigated the ability of monochloramines and dichloramines of small peptides to kill bacteria. At 10 nmoles, monochloramines were unable to kill 10^5 *S. aureus*. The majority of the dichloramines were cytotoxic with LD₅₀s of approximately 2.5 nmoles, but they lost activity with time. Dichloramines that did not have an amino acid substituent, such as taurine dichloramine and glycine dichloramine, were not bactericidal up to 10 nmoles per 10^5 *S. aureus*. Dichloramines were much more unstable than their related monochloramines. Stability was related to the amino acid substituent. Monochloramines broke down to yield non-toxic aldehydes. Decomposition of dichloramines occurred via multiple, competing pathways forming non-toxic *N*-chloroiminopeptides and other unidentified products. Volatile ammonia (NH₃), ammonium monochloramine (NH₂Cl) and ammonium dichloramine (NHCl₂) were detected in the headspace using selected ion flow tube mass spectrometry. Chlorinated ammonia was cytotoxic with LD₅₀s in the order of NHCl₂ (0.08 ± 0.02 nmoles) <HOCl (0.14 ± 0.04 nmoles) <NH₂Cl (0.37 ± 0.14 nmoles). The other products were not bactericidal. We propose that HOCl will react with amine groups within neutrophil phagosomes to form unstable dichloramines. These will then liberate cytotoxic NH₂Cl and NHCl₂, which will contribute to neutrophil oxidative killing of bacteria.