New Developments in Lantibiotic Biosynthesis and Mode of Action

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Lantibiotics are a class of peptide-derived antimicrobial agents. They are ribosomally synthesized as inactive precursor peptides that subsequently undergo post-translational modification by a multienzyme complex to their mature, biologically active forms. All lantibiotics contain lanthionine and/or methyllanthionine residues and also typically the unsaturated amino acids dehydroalanine and dehydrobutyrine. These structural motifs are the bases for their function. The lantibiotic haloduracin consists of two post-translationally processed peptides, Halα and Halβ, that act in synergy to provide bactericidal activity. The recently developed *in vitro* haloduracin production system was utilized to examine the biological impact of individual thioether ring disruption in each peptide. In other studies, the unique structure and potential for beneficial pharmaceutical applications of the lantibiotic cinnamycin have led us to investigate its biosynthesis. Cinnamycin is a tetracyclic lantibiotic that contains one lanthionine, two methyllanthionines, a β-hydroxy-aspartate residue, and a lysinoalanine linkage. The activities of the lantibiotic modifying enzyme, CinM, and the aspartate hydroxylase, CinX, have been successfully reconstituted *in vitro*. Formation of the lysinoalanine linkage and bioactivity assays are currently under investigation.