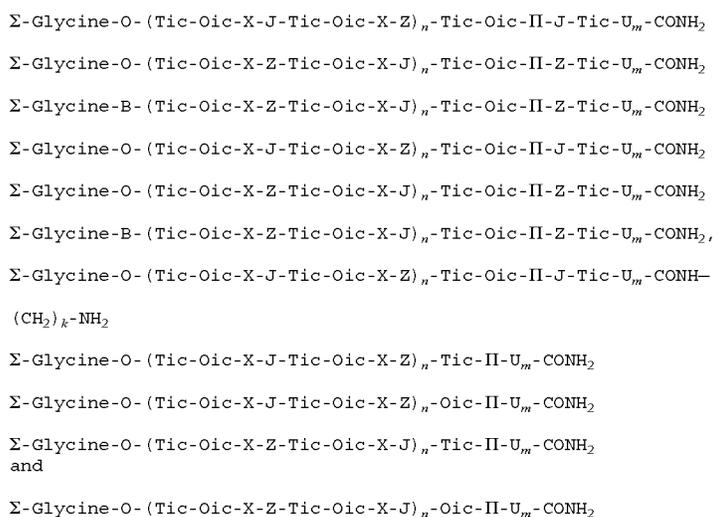


designed a new class of AMPs with increased potency and selectivity for one or more specific strains of bacteria.

[0008] As a source of new drugs, the inventors have explored naturally occurring peptides that exhibit antimicrobial activity via membrane disruption. They have designed, synthesized and evaluated a new class of novel antimicrobial peptides containing un-natural amino acids, which AMPs exhibit increased potency and selectivity against Gram positive, Gram negative and *Mycobacterium*—and unexpectedly many of the new AMPs also exhibit reduced hemolytic activity. These new compounds were designed based on the electrostatic surface potential maps derived from the SDS and DPC micelle-bound conformations of (Ala^{8, 13, 18})magainin-2-amide, as described in more detail below. Un-natural amino acids were incorporated into the polypeptide backbone to control the structural and physicochemical properties of the peptides to introduce organism selectivity and potency. The

inventors discovered that un-natural amino acid residues increase the resistance to proteolytic or enzymatic degradation, thus providing improved stability in biological systems over AMPs consisting of only natural amino acids. Such peptides may be referred to as peptidomimetic. The term “peptidomimetic” denotes a small protein-like chain synthetically designed to mimic a natural peptide, as for instance, where a natural peptide is modified to alter the peptide’s properties. Typically, changes include those that will not occur naturally (such as altered backbones and the incorporation of non-natural amino acids).

[0009] More particularly, the inventors discovered that a synthetic antimicrobial peptide analog having one of the following (referred to hereafter as General Formulae) were effective against at least one of Gram positive, Gram negative and *Mycobacterium*, and preferably (but not necessarily) exhibit reduced hemolytic activity.



[0010] In addition, one preferred embodiment of the AMPs is encompassed by the following, which are referred to as the “Tic-Tic analogs”. As shown below, these analogs exhibit greater selectivity for *Mycobacterium ranae*, compared to Gram positive and Gram negative bacteria.

