



## Mini Review on Antimicrobial Peptides, Sources, Mechanism and Recent Applications



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**Abstract:** Antimicrobial peptides in recent years have gained increased interest among scientists, health professionals and the pharmaceutical companies owing to their therapeutic potential. These are low molecular weight proteins with broad range antimicrobial and immuno modulatory activities against infectious bacteria (Gram positive and Gram negative), viruses and fungi. Inability of micro-organisms to develop resistance against most of the antimicrobial peptide has made them as an efficient product which can greatly impact the new era of antimicrobials. In addition to these peptides also demonstrates increased efficacy, high specificity, decreased drug interaction, low toxicity, biological diversity and direct attacking properties. Pharmaceutical industries are therefore conducting appropriate clinical trials to develop these peptides as potential therapeutic drugs. More than 60 peptide drugs have already reached the market and several hundreds of novel therapeutic peptides are in preclinical and clinical development. Rational designing can be used further to modify the chemical and physical properties of existing peptides. This mini review will discuss the sources, mechanism and recent therapeutic applications of antimicrobial peptides in treatment of infectious diseases.

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### 1. INTRODUCTION

Antimicrobial Peptides (AMPs) are low molecular weight proteins with broad spectrum antimicrobial and immuno modulatory activities against infectious bacteria (Gram positive and Gram negative), viruses and fungi [1]. These antimicrobial peptides have been classified according to their physiochemical properties like net charge, secondary structural contents and solubility [2]. AMPs contain both hydrophobic and hydrophilic side chain that enables these molecules to be soluble in aqueous environments [3]. Amongst the most abundant and widespread AMPs in nature, the cationic alpha-helical AMPs are able to perturb the bacterial cytoplasmic membrane causing cell death by osmotic shock. Some of the most important class of AMPs in these groups are cecropin, magainin, the human cathelicidin LL-37, their derivatives and proline rich Antimicrobial Peptides (prAMPs) [4-12]. Besides cationic AMPs, anionic AMPs have also been described [13]. One positive feature of AMPs is their low propensity towards developing resistance which may be attribute to its distinguished mode of action on the plasma membrane, where it natively folds into three dimensional amphiphilic structure that causes bacterial cell disruption, as documented in previous studies [14, 15]. These

peptides initially interact with the bacterial cell envelope, and later translocates to cytosol [16, 17]. And unlike common antibiotics, AMPs do not inhibit peptidoglycan synthesis by binding with proteins; rather create pores in membrane forming complex with precursor molecule present in the membrane [18, 19]. Antimicrobial peptides are diverse group of proteins divided into many subgroups on the basis of their amino acid composition and structure and other properties [20, 21]. The secondary structures of these short peptide may have four architectures that include i)  $\alpha$ -helical, ii)  $\beta$ -stranded due to the presence of 2 or more disulfide bonds, iii)  $\beta$ -hairpin or loop due to the presence of a single disulfide bond and/or cyclization of the peptide chain, and iv) extended [22]. AMPs participate in the innate immune response by providing rapid first line defence against infection [1]. This review will focus and report various sources of antimicrobial peptides, variety of structure, mechanisms of action and therapeutic interventions of antimicrobial peptides.

### 2. SOURCES OF AMPs

Discovery of AMPs dates back to 1939, when Dubos extracted an antimicrobial agent from a soil *Bacillus* strain. After that several AMPs have been discovered from both the prokaryotes and eukaryotes [23-25], frog skin alone is source of more than 300 different AMPs [24]. Recently, scientists from Japan have successfully explained the molecular

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mechanism of antimicrobial peptides, Bombinins H2 and H4 discovered from skin secretions of frog species *Bombina variegata*. Both these antimicrobial peptides have shown promising ability to inhibit highly infectious and fatal disease called Leishmaniasis. Mechanism of action of these peptides will enable us to better understand how defence system of the frog has evolved and how this can be implemented in developing antimicrobial peptides against important microbial infections. It was reported that Leishmania affect almost 20 million people worldwide and is the cause of approximately 30,000 deaths each year [26]. Other AMPs discovered are defensin from rabbit leukocytes [27], lactoferrin from cow milk [28], lysosomes of human leukocytes [29] and low molecular weight antimicrobial peptide from human female reproductive tract [30]. Several *Bacillus* strains producing antimicrobial peptides have been identified which have shown promising inhibitory activity against *Shigella*, *Salmonella*, *E. coli* and *Staphylococcus aureus* [31-34]. In another study, an antimicrobial peptide reported from *Bacillus* sp. [31, 32] found to be active against *Staphylococcus aureus*, *Alteromonas* sp. strain CSH174 and *Klebsiella pneumoniae*. An extracellular antimicrobial peptide has also been discovered from *Propionibacterium jensenii* [35]. Antimicrobial peptides isolated from *Pseudomonas* [33] showed activity against *Shigella*, *Salmonella*, *E. coli*, *Staphylococcus aureus*. Another peptide which as shown high inhibitory activity against bio film was discovered in year 2015 [36].

Researchers have also modified lactoferrin of bovine at the N-terminal domain that demonstrated high activity against multidrug-resistant bacteria and *Candida* [37]. Antimicrobial Peptide Database (APD) contains entry of ~2981 antimicrobial peptides from six kingdoms (335 bacteriocins/peptide antibiotics from bacteria, 4 from archaea, 8 from protists, 13 from fungi, 342 from plants, and 2200 from animals, including some synthetic peptides, in total, more than 5,000 AMPs have been discovered or synthesized till date [38]. More recently, glycocin, a small antimicrobial peptide was discovered from thermophilic bacterium which was found to be stable at relatively high temperatures, the gene encoding glycocin was successfully transformed in *E. coli* bacterium [39]. Table 1 further summarizes discovery of various AMPs from variety of organisms [40-88].

### 3. INSIGHTS INTO MECHANISM OF ACTION OF AMPs

Antimicrobial peptides interact with bacterial cell membrane through electrostatic interactions [89] thus making it difficult for bacteria to develop resistance unlike conventional antibiotics [90]. Based on their mode of action, these peptides are classified into membrane acting and non membrane acting peptides. Membrane acting peptides mainly harbour cationic peptides causing membrane disruptions, whereas non membrane peptides are capable of translocation across the membrane without damaging it as also reviewed in previous study [91]. Few antibacterial peptides create trans-membrane pores on the target membrane and include defensin [92], melittin [93], aganin [94], and LL-37 [95]. Antimicrobial peptides such as buforin II [82], dermaseptin [96], HNP-1 [97], pleurocidin [98],

indolicidin [99], pyrrolicidin [100], and mersacidin [101] these peptides translocates across the cell membrane and disrupt normal cell functioning [102]. Outer membrane of prokaryotic cell is negatively charged owing to presence of lipopolysaccharides or teichoic acid, whereas the outer leaflet of eukaryotic cell consists of zwitterionic phosphatidylcholine and sphingomyelin phospholipids. Cationic AMPs interact with negatively charged outer microbial membranes via selective interactions [103], and attain well-defined secondary structures, makes cell permeable and finally disrupt bacterial membranes [15]. These peptides show dynamics in structure and topologies during their interactions with the microbial cell membranes [104, 105].

AMPs also hamper processes like protein synthesis, nucleic acid synthesis, enzymatic activities, and cell wall synthesis [106-108]. Several factors that include magnitude and charge of the outer membrane, concentration of negatively charged molecules, molecular architecture, and membrane fluidity are essential for the transportation of peptide across the membrane [109]. The membrane fluidity also regulates adsorption and insertion of AMPs into the cell membrane. Malanovic and Lohner in year (2016) studied antimicrobial peptides against Gram positive bacteria and found that prior targeting the cytoplasmic membrane these peptides cross the cell wall components such as lipoteichoic acids and peptidoglycan [110]. It was established that highly conserved precursors of cell wall components, especially lipid II are directly targeted by AMPs [111]. Majority of these antimicrobial peptides fold into amphipathic conformations while interacting with membrane [112]. Some of the antimicrobial peptides crosses lipid bilayer, target intracellular components, binds DNA, block enzyme activity, inhibit synthesis of proteins, cell wall, and nucleic acids [113, 114]. AMPs thus displays antibacterial efficacy because of intracellular inhibitory mechanisms. Unfortunately, these aspects remain elusive, various models used to explain the AMP mechanism of action on bacterial membrane are *Barrel-stave mechanism* [115] *Carpet model* [116] and *Toroidal pore model* [117] (Figure 1).

Despite all reported evidences, the mechanism of action and disruption of membranes is not fully understood. Some examples of antimicrobial peptides showing intracellular activities are reported in Table 2 [118-121].

### 4. APPLICATIONS OF AMPs

#### 4.1. Application in Ophthalmology

AMPs are being employed in ophthalmology, a previous study reported use of rabbit alpha defensin (NP-1) against several ocular infections [122]. Recently, a cecropin analogue, Hecate has also shown inhibitory action against many *Acanthamoeba* species *in vitro*. Among other tested cecropin analogues SHIVA-11 is widely used against various ocular infections [123]. Table 3 further summarizes examples of peptides and their activity against relevant pathogens in ocular infections.

#### 4.2. Treatment of Local Infections

Several peptides have been used in treating local infections, a peptide NEUPREX (rBPI21, opebacan) is

**Table1.** List of antimicrobial peptides from different sources.

AMPs from Insects					
S. No.	Peptide Name	Source	Amino Acid Number	Antimicrobial Activity	References
1	Acaloleptin	<i>Acalolepta luxuriosa</i>	71	G <sup>+</sup> , G <sup>-</sup>	[40]
2	Andropin	<i>Drosophila melanogaster</i>	34	G <sup>+</sup>	[41]
3	Apidaecin IA	<i>Apis mellifera</i>	18	G <sup>-</sup>	[42]
4	Cecropin	<i>Hyalophora cecropia</i>	37	G <sup>-</sup>	[43]
5	Defensin- $\alpha$	<i>Aedes aegypti</i>	40	G <sup>+</sup> , G <sup>-</sup>	[44]
6	Drosomyacin	<i>Drosophila melanogaster</i>	44	F	[45]
7	Holotricin	<i>Holotrichia diomphalia</i>	43	G <sup>+</sup> , G <sup>-</sup>	[46]
8	Sapecin- $\alpha$	<i>Sarcophaga peregrine</i>	40	G <sup>+</sup> , G <sup>-</sup>	[47]
9	Tenicin 1	<i>Tenebrio molitor</i>	43	G <sup>+</sup> , G <sup>-</sup>	[48]
10	Thanatin	<i>Podisus maculiventris</i>	21	G <sup>+</sup> , G <sup>-</sup>	[49]
From Humans					
1	Cathelicidins	Human neutrophils	30	F, G <sup>-</sup> , G <sup>+</sup>	[50]
2	A Defensins	Human neutrophils	12-80	F, G <sup>-</sup> , G <sup>+</sup>	[51]
3	Human Histatin 8	<i>Homo sapiens</i>	12	F, G <sup>-</sup> , G <sup>+</sup>	[52]
4	LL37	Neutrophils ( <i>Homo sapiens</i> )	37	F, G <sup>-</sup> , G <sup>+</sup>	[53]
From Animals					
1	Androctonin	<i>Androctonus australis</i>	25	F, G <sup>-</sup> , G <sup>+</sup>	[54]
2	Bactenecin	Bovine Neutrophils	12	G <sup>-</sup> , G <sup>+</sup>	[55]
3	Brevinin	<i>Rana brevipora porsa</i>	24	G <sup>-</sup> , G <sup>+</sup>	[56]
4	Bufoforin II	<i>Bufo bufo gargarizans</i>	21	F, G <sup>-</sup> , G <sup>+</sup>	[57]
5	Cupiennin	<i>Cupiennius salei</i>	35	G <sup>-</sup> , G <sup>+</sup>	[58]
6	Dermaseptin S1	<i>Phyllomedusa sauvagii</i>	34	G <sup>-</sup> , G <sup>+</sup>	[59]
7	Lycotoxin	<i>Lycosa carolinensis</i>	27	G <sup>-</sup> , G <sup>+</sup>	[60]
8	Tachyplesins	<i>Tachyplesus tridentatus</i> (Horseshoe crab)	17	G <sup>-</sup>	[61]
From Plants					
1	Hevein	Latex of rubber trees	43	F	[62]
2	Purothionins	Wheat endosperm	45	G <sup>+</sup> , G <sup>-</sup>	[63]
From Microorganisms					
1	Nisin	<i>Lactococcus lactis</i>	34	G <sup>+</sup>	[64]
2	Alamethicin	<i>Trichoderma viride</i>	20	G <sup>+</sup>	[65]
3	Enterocin	<i>Enterococcus</i>	70	G <sup>+</sup> , G <sup>-</sup>	[66]
4	Hominicin	<i>Staphylococcus hominis</i> MBBL 2-9	21	G <sup>+</sup> , G <sup>-</sup>	[67]
5	Ericin S	<i>Bacillus subtilis</i>	32	G <sup>+</sup>	[68]
6	Plantaricin A	<i>Lactobacillus plantarum</i>	26	G <sup>+</sup> , G <sup>-</sup>	[69]
7	Carnobacteriocin B2	<i>Carnobacterium piscicola</i>	48	G <sup>+</sup> , G <sup>-</sup>	[70]

Table 1 contd....

S. No.	Peptide Name	Source	Amino Acid Number	Antimicrobial Activity	References
8	Leucocin A	<i>Leuconostoc pseudomesenteroides</i>	37	G <sup>+</sup> , G <sup>-</sup>	[71]
9	Subtilin	<i>Bacillus subtilis</i>	32	G <sup>+</sup>	[72]
10	Pyricularia thionin	<i>Pyricularia pubera</i>	47	G <sup>+</sup> , G <sup>-</sup>	[73]
11	Microcin J25	<i>Escherichia coli</i> AY25	21	G <sup>-</sup>	[74]
12	Gramicidin A	<i>Bacillus brevis</i>	15	G <sup>+</sup> , G <sup>-</sup>	[75]
13	Pediocin PA-1/ AcH	<i>Pediococcus acidilactici</i> PAC-1.0	44	G <sup>+</sup>	[76]
14	Mesentericin Y105	<i>Leuconostoc mesenteroides</i>	37	G <sup>+</sup>	[77]
15	Carnobacteriocin BM1	<i>Carnobacterium piscicola</i> LV17B	43	G <sup>+</sup> , G <sup>-</sup>	[78]
16	Streptin 1	<i>Bacillus subtilis</i> A1/3	23	G <sup>+</sup>	[79]
17	Planosporicin	<i>Planomonospora alba</i>	24	G <sup>+</sup> , G <sup>-</sup>	[80]
18	Gassericin A	<i>Lactobacillus gasseri</i> LA39	58	G <sup>+</sup> , G <sup>-</sup>	[81]
19	Circularin A	<i>Clostridium beijerinckii</i> ATCC 25752	69	G <sup>+</sup> , G <sup>-</sup>	[82]
20	Divercin V41	<i>Carnobacterium divergens</i> V41	43	G <sup>+</sup>	[83]
21	Listeriocin 743A	<i>Listeria innocua</i> 743	43	G <sup>+</sup>	[84]
22	Plantaricin C19	<i>Lactobacillus plantarum</i> C19	37	G <sup>+</sup>	[85]
23	Enterocin P	<i>Enterococcus faecium</i> P13	44	G <sup>+</sup>	[86]
24	Subtilosin A	<i>Bacillus subtilis</i>	35	G <sup>+</sup> , G <sup>-</sup>	[87]
25	Plantaricin ASM1	<i>Lactobacillus plantarum</i> A-1	43	G <sup>+</sup>	[85]
26	Lichenin	<i>Bacillus licheniformis</i>	12	G <sup>+</sup> , G <sup>-</sup>	[88]

F – Fungus; G<sup>+</sup> - Gram positive; G<sup>-</sup> - Gram negative.

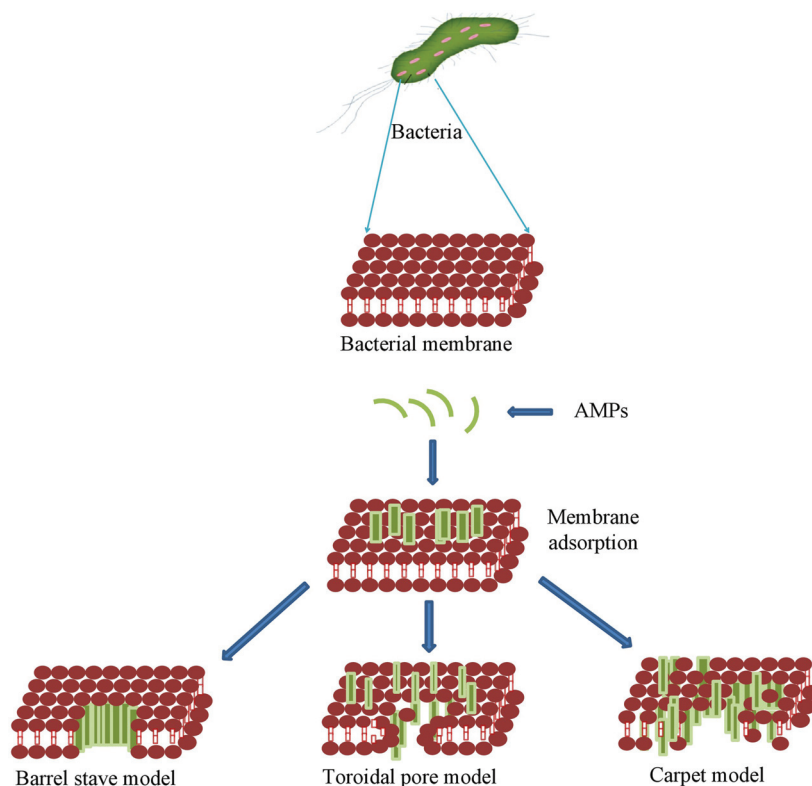


Figure 1. Various models demonstrating mechanism of action of AMPs.

**Table 2. Antimicrobial peptide displaying intracellular membrane activities.**

S. No.	AMPs	Intracellular Target	References
1	Buforin II, tachyplesin	Binds to DNA	[118]
2	Pleurocidin, dermaseptin, PR-39, HNP-1, HNP-2, Indolicidin	Inhibits DNA, RNA and protein synthesis	[119]
3	Histatins, pyrrolicocin, Drosocin, Apidaecin	Inhibits enzymatic activity	[18]
4	<i>N</i> -acetylmuramoyl-L-alanine Amidase	Activation of autolysin	[120]
5	PR-39, PR-26, indolicidin, microcin 25	Alters cytoplasmic membrane (inhibits septum formation)	[121]
6	Mersacidin	Inhibits cell-wall Synthesis	[100]

**Table 3. Inhibitory activity of antimicrobial peptides and proteins against relevant pathogens in ocular infections.**

Protein/Peptide	Microorganisms	References
HB43, HB55, HBPM4	<i>Staphylococcus aureus</i>	[130]
HBCM2, HBCM3, HB14	<i>Pseudomonas aeruginosa</i>	[131]
Lactoferrin	<i>Haemophilus influenzae, Staphylococcus, epidermidis, Pseudomonas spp.</i>	[132]
Lactoferricin B	<i>Aspergillus fumigatus, Candida albicans</i>	[14]
Mucins	<i>Candida spp., P. aeruginosa</i>	[43, 133]
NP-1	<i>C. albicans, Streptococcus pneumoniae, P. aeruginosa</i>	[134]
Protegrin-1	<i>S. aureus, P. aeruginosa</i>	[135]
Shiva-11	<i>S. aureus, S. pneumoniae, P. aeruginosa</i>	[136]
Thiazomycin A	<i>S. aureus</i>	[115]
COL-1	<i>Pseudomonas</i>	[137]

injectable preparation of rBPI21 used in treatment of paediatric patients undergoing open heart surgery and patients with severe burns [124]. A recombinant peptide HBD-2 is being used in eliminating the infections attained during the use of prosthetics implantation [125]. Peptides derived from amphibian skin *e.g.* alyteserin, brevinin, ascaphin, pseudin, kassinatuerin and temporin have been effectively used in the treatment of local infections caused by multi-drug resistant strains of bacteria *e.g.* *Acinetobacter baumannii* strains, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida sp.* [126]. P113 is another peptide naturally occurring in saliva [10], which display high *in vitro* activity against *Candida albicans* and commonly occurring Gram-positive and Gram-negative pathogens, it is also being used in the form of a mouthwash for the treatment of oral *Candidiasis* in HIV patients [127]. Pexiganan is first antimicrobial peptide used in the form of an ointment for treating local infection encountered during diabetic foot

ulcers [128]. Variants of indolicidin-based peptide, MX-226 and MX-594AN (omiganan pentahydrochloride, 1% gel) are being used in treating infections associated with the use of catheters and against treatment of *Acne vulgaris* respectively [129]. Another peptide MBI-853NL is being used in preventing infection associated with Methicillin-Resistant Strains (MRSA), it also eliminates their carriage to nasal cavity [122]. IB-367 is a variant of porcine protegrin-1 which is used in treatment of oral mucositis, a side-effect of anticancer therapies with 'mixed' infections in the mouth.

## 5. AMPs IN CLINICAL TRIALS

Due to numerous advantages of antimicrobial peptides such as high potency, efficacy selectivity, broad range targets, potentially low toxicity and low accumulation in tissues, pharmaceutical industries aims to develop them as therapeutic drugs and appropriate clinical trials therefore are

**Table 4. Peptide antibiotics in clinical trials.**

Peptide	Company	Clinical Trial Phase	Spectrum/Mode of Action	References
CZEN-002	Zengen	Phase I/II	GPB, GNP, Candida. Yeast regulatory mechanisms, Interference by cAMP induction, anti-inflammatory.	[155]
Daptomycin	Cubicin	In market	GPB. Depolarisation of membrane potential, inhibition of protein, DNA and RNA synthesis.	[156]
EA-230	Exponential biotherapies	Phase I/II	Anti-inflammatory. Sepsis and renal failure protection.	[157]
Pexiganan (MSI-78)	Genaera Corporation	Phase III	Infected diabetic foot ulcers	[158]
Omiganan	MIGENIX	Phase II/III	Catheter infections and rosacea	[159, 160]
Lytixar (LTX-109)	Lytix Biopharma	Phase I/II	Uncomplicated Gram positive skin infections, impetigo, and nasal colonization with <i>S. aureus</i>	[130]
hIF1-11	AM-Pharma	Phase I/II	Bacteraemia and fungal infections in immunocompromized haematopoietic stem cell transplant recipients	[161]
Novexatin (NP-213)	NovaBiotics	Phase II	Onychomycosis (fungal nail infection)	[162]
LL-37	Karolinska Institute	Phase I/II	Hard-to-heal venous leg ulcers	[163]
PAC-113	Demegen	Phase II	Oral candidiasis in HIV seropositive patients	[130]
RDP-58	Genzyme	Post Phase II	Inflammatory bowel disease	[164]
MX-594AN	Migenix	Phase II	Topical treatment for <i>Acne vulgaris</i>	[165]
MX-226	Migenix	Phase III b	Dermatology related infections	[153]
HB-1345	BioMedix	Pre-Phase I	Acne	[166]
HB-107	Biopharmaceuticals	Preclinical	Wound healing	[167]
Glutoxim	Pharma BAM	Phase II	Tuberculosis	[168]
IMX942	Inimex	Phase I A	Immunomodulation, Treatment of fevers in chemotherapy patients	[158]
DPK-060	Promore Pharma	Phase II	Treatment of atopic dermatitis	[169]
POL7080	Polyphor Ltd	Phase II	Treatment of non-cystic fibrosis bronchiectasis	[170]
SB006	SpiderBiotech (Italy)	Preclinical	Antidotoxigenic activity	[171]
PL-5	China Food and Drug Administration (CFDA)	Phase II	Treatment of skin infections	[172]

being conducted [138]. More than 60 peptide drugs have reached the market and several hundred novel therapeutic peptides are in preclinical and clinical development [139] (Table 4). Emerging peptide technologies, including multifunctional peptides, cell penetrating peptides and peptide drug conjugates will widen the application of peptides as therapeutics [140]. United States of America dominates the global production and commercialization of peptide drug followed by Europe. Companies like Theravance and Vicuron Pharmaceuticals are the major

American companies largely dedicated in the development of peptide antibiotics [141]. However, certain peptides could not have entered clinical trials, MSI-78 (pexiganan acetate, which is a potent antimicrobial peptide designed from Magainin) was a prominent failure that has entered phase III of clinical trials and showed efficacy against diabetic foot ulcer infections [43], however, in July 1999, the FDA disapproved use of Magainin based on inadequacy trial design. Isegran IB-367, a synthetic protegrin analogue failed Phase III clinical trials as mouth rinse for stomatitis in

high risk patients owing to aerosolized Rx in ventilator-associated pneumonia [142]. The trial achieved its secondary endpoint for reduction of pain but did not meet the primary end point for presence of ulceration. Nevertheless, this trial continues to enroll patients for a second phase III trial [143]. Micrologix Biotech Inc. has introduced 3 separate antimicrobial peptides related to indolicidin into clinical trials [144]. The most advanced peptide MBI-226 [115] has entered phase III clinical trials for preventing catheter-related bloodstream infections. According to company press releases and conference presentations, preclinical studies demonstrated that MBI-226 is effective in animal models, it has successfully reduced the skin colonization by variety of bacteria causing catheter-related infections [145], and also demonstrated good antifungal activity against *Candida albicans* in guinea pig skin [146]. A randomized, double-blind phase I clinical trial in 18 healthy volunteers demonstrated that MBI-226 was safe, well tolerated and eliminated 99.9% of common skin bacteria for prolonged periods [147]. Furthermore, it completely prevented short-term Central Venous Catheter (CVC) colonization. Since CVC colonization is a common cause of serious life-threatening infections in hospitalized patients, causing 90% (180,000/year) of bloodstream infections that results in an average of 6.5 additional days of intensive care and up to 50,000 deaths annually [148], Micrologix received fast track status from the FDA and initiated two clinical trials using indolicidin-like peptides for treatment of acute acne (in phase II clinical trials) and killing MRSA in the nares (in phase Ib trials) [149, 150].

All over, use of AMPs have proven to be successful in treating infections, in fact, antimicrobial peptide have already entered the global market *e.g.* magainin is being used in treating viral and bacterial diseases [151, 152]. Several studies carried out globally by researchers have provided in depth understanding about antimicrobial peptides mechanism, efficacy, safety, and other related concern and has helped in creating online database service as well as the future potential of AMPs [22, 153, 154]. Incontestable need for new ways to manage infections and the proven importance of peptides in innate immunity should render the investment worthwhile for human medicine. The research investments are needed to bring more peptide antibiotics to the clinic will likely remain substantial in the foreseeable future. As described below, a number of AMPs and AMP derivatives are already at the pre-clinical stage and in clinical trials.

## CONCLUSION

Antimicrobial resistance is multifaceted, multi-dimensional, and is second largest cause of deaths in the world. Both the Gram positive and Gram negative bacteria are getting refractory to current armamentarium of antimicrobial drugs. Treatment of bacterial infections caused by MDR strains that include vancomycin-resistant *Enterococcus faecium*, *Enterobacter cloacae* (MRSA), XDR strains that include carbapenem-resistant *Acinetobacter baumannii*, and third generation cephalosporin resistant *E. coli*,  $\beta$ -lactamase producing *Klebsiella pneumoniae*, carbapenem-resistant *Klebsiella pneumoniae*, carbapenem-resistant *Pseudomonas aeruginosa* and *Mycobacterium* has

become quite difficult. All living organisms are constantly threatened by large numbers of microorganisms seeking to exploit the same environmental space. To cope with this substantial microbial threat, most cells produce natural antibiotic like molecules that directly kill or inhibit the growth of foreign microorganisms. The urgent need to obtain new antimicrobials has been driving AMP research. In this respect, AMPs are considered as promising antimicrobial agents for producing new generation antimicrobials. Although there are several obstacles to be overcome for clinical applications, natural and synthetic AMPs are still attractive sources to the pharmaceutical companies. In order to facilitate commercial development of peptide antibiotics, it is reasonable to focus on small peptides.

## LIST OF ABBREVIATIONS

AMPs	=	Antimicrobial Peptides
<i>E. coli</i>	=	<i>Escherichia coli</i>
APD	=	Antimicrobial Peptide Database
sp.	=	Species
prAMPs	=	proline rich Antimicrobial Peptides
F	=	Fungus
G <sup>+</sup>	=	Gram positive
G <sup>-</sup>	=	Gram negative
DNA	=	Deoxyribonucleic Acid
RNA	=	Ribonucleic Acid
<i>e.g.</i>	=	exempli gratia
HIV	=	Human Immunodeficiency Virus
MRSA	=	Methicillin-Resistant <i>Staphylococcus aureus</i>
<i>P. aeruginosa</i>	=	<i>Pseudomonas aeruginosa</i>
<i>C. albicans</i>	=	<i>Candida albicans</i>
<i>S. aureus</i>	=	<i>Staphylococcus aureus</i>
<i>S. pneumoniae</i>	=	<i>Streptococcus pneumoniae</i>
FDA	=	Food and Drug Administration
CVC	=	Central Venous Catheter
cAMP	=	Cyclic Antimicrobial peptides
MDR	=	Multidrug-Resistant
XDR	=	Extensive Drug Resistant

## CONSENT FOR PUBLICATION

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## CONFLICT OF INTEREST

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