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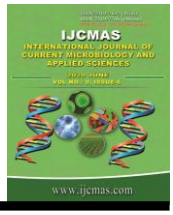

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Anti-microbial Peptides: New Weapon against Bacteria

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A B S T R A C T

Antimicrobial peptides (AMPs), also known as host defense peptides, are short and generally positively charged peptides found in a wide variety of life forms from microorganisms to humans. Most AMPs have the ability to kill microbial pathogens directly, whereas others act indirectly by modulating the host defense systems. Against a background of rapidly increasing resistance development to conventional antibiotics all over the world, efforts to bring AMPs into clinical use are accelerating.

Introduction

20th Century was marked by the undeniable success in the field of treatment and prophylaxis of infectious diseases. However with advancements in treatment protocols and drugs being used, the bacteria are also evolving. The spread of drug-resistance is of major concern and poses a serious threat to the existing medial doctrine founded on the effective use of antibiotics. In 2015, the Global Action Plan on anti-microbial resistance was endorsed at the 68th World Health Assembly which emphasizes more on development of new compounds and methods effective against multi-drug resistant microbes.

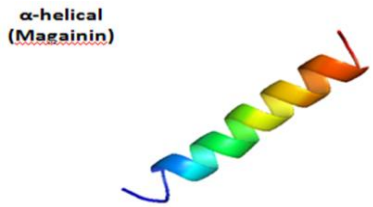
Anti-microbial peptides

They are evolutionary conservative tools of the innate immunity providing immediate response to a large set of various pathogen. They were firstly discovered by Dubos in 1939 from soil bacillus. Hotchkins and Dubos fractioned and identified it as Gramicidine. AMPs are oligopeptides are generally cationic and amphipathic molecules with varying number of amino acids with a broad spectrum of target range.

So far more than 800 AMPs have been discovered.

Structure

∝-Helical symmetry



Contains 12-40 amino acid residues and helix stabilizing residues such as alanine, leucine and lysine but never cysteine.

β-sheet symmetry

Typically contains 2-10 cysteine residues that from intrachain disulphide bonds which allows then adopt the ***β*-sheet** conformation.

Loop structures

Proline and arginine rich peptides. They cannot form amphipathic structure. Rather they form polyproline type II structure. The peptides of their group are of great interest due to their short sizes, proteolytic stability and ease of synthesis.

Other structures

Rich in certain specific amino acids.
For example- Histatine- peptide rich in histidine residues.

Some anti-microbial peptides and their sources

TABLE 1: Representative antimicrobial peptides of different classifications (modified from [13]).

Class	Representatives	Host
α-helical	LL-37	Mammal: human
	Cecropins	Insect: moth
	Melittin	Insect: honey bee
	Magainins	Amphibian: frog
	Fowlicidins	Ave: chicken
β-sheet	Thanatin	Insect: soldier bug
	Tachyplesins	Arthropod: horseshoe crab
	Protegrins	Mammal: pig
	Plant defensin VrD2	Plant: mung bean
	Plectasin	Fungus: ebony cup
	Insect defensin A	Insect: northern blow fly
	α-defensin	Mammal: human
	β-defensin	Mammal: human
	θ-defensin	Mammal: rhesus monkey
Flexible	Indolicidin	Mammal: cow
	Tritrpticin	Mammal: pig
	Histatins	Mammal: human
	PR-39	Mammal: pig

Classification of AMPs based on the ionic structure

Classification of AMPs

CLASS	EXAMPLE	STRUCTURE	ORIGIN
Anionic peptides	Dermicidin	Asp & Glu	Human
Cationic peptides	Cecropin	Helical	*insects*
	LL37	Helical	Human
Cationic peptides with specific amino acids	PR 39	Pro & arg rich	Pig
	Prophenin	Pro & Phe	Pig
	Indolicidin	Trp rich	cattle

Cont….

Peptides that forms disulphide bridges	Brevinins	1-disulphide bridge	Amphibians
	Tachyplesin	2-disulphide bridges	Horse shoe crab
	Defensins	3-disulfide bridges	Human
	NK-lysin	3-disulfide bridges	Pig
	Drosomycin	More than 3-disulfide bridges	Fruitfly
Fragmented peptides	Lactoferricin	14-42 a.acids	Human

Mechanism of action

The basic mechanism of action of anti-microbial peptides is the alteration of cell membrane permeability which leads to the loss of cellular components resulting into cell death.

Variation models have been proposed to the prevailing concepts of mechanism of action on anti-microbial peptides.

The following mechanism of action is being followed –

Barrel-Stave model

Formation of transmembrane channels or pores by bundles of peptides.

During binding, hydrophobic residue/surface of alpha-helical and beta-sheet peptides face outwards whereas the hydrophilic surface for the pore-lining. After binding these peptides undergo conformational changes, facing the polar phospholipids head group to align, thus inducing membrane thining eventually leading to leakage and cell death.

Carpet model

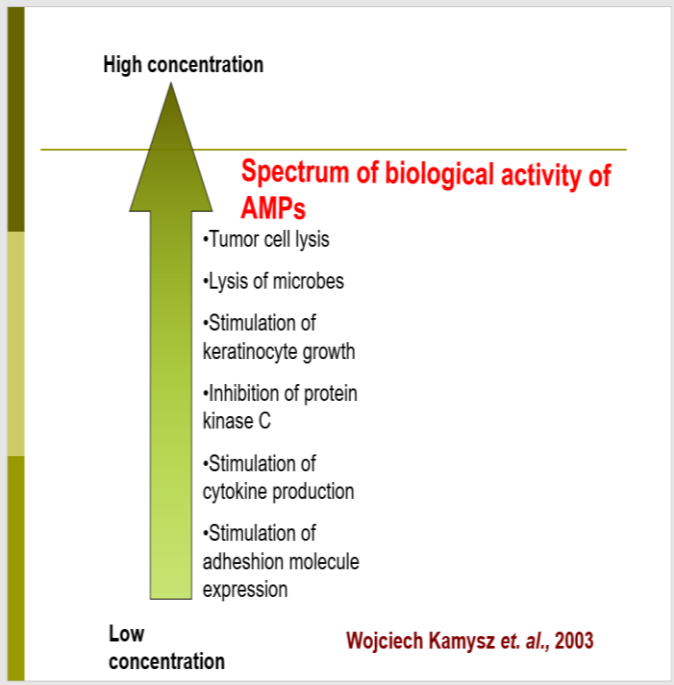
Due to electrostatic binding, the peptides cover the membrane like a carpet and when the electrostatic interaction reaches a threshold concentration, peptides cause membrane permeation leading to lysis of microbial cell.

Torroidal pore

Represents a membrane spanning pore lined with polar peptide surface and phospholipids head group. The alpha-helicals like magainins and PGA act by this mechanism. The hydrophobic residues bond peptides displace polar head groups thus creating a breach in hydrophobic region of membranes.

Anti-microbial peptides and their uses

Plays a major role in maintenance of innate immunity



Therapeutic potential

Magainin pharmaceutical Inc. have taken the **α**-helical magainin variant MSI-78 into Phase-III clinical trials to test it's efficacy against polymicrobic foot ulcer infection in diabetes

Trials initiated to test Lantibiotic Nisin against *Helicobacter pyroli* in stomach cancer.

α-helical peptide SMAP29 is effective against *P.aeruginosa* in peritoneal infections.

Beta sheet protregrins is effective against MRSA, VRE and *P.aeruginosa*.

Food preservation and as a feed additive

Peptides such as PR-39 have been shown to inhibit the growth of *S. typhimurium* by interfering with it's DNA synthesis.

Similarly another peptide named Sphenicin has action against many gram positive and negative bacteria and thus helps in decreasing microbial spoilage of food.

Similarly there are peptides such as protamine and magainins which have almost identical mechanism of action and reduce food spoilage.

Feed additive

In a recent study on piglets, it was concluded that antimicrobial peptides can also be used as a feed additive.

Piglets were fed a diet rich in antimicrobial peptides such as AMP-P5, Cercopins, Colicin, Lactoferrin.

All of them showed a positive effect on immune status of the animals, and apparent digestibility and also reduced the quantity of coliforms from the digestive tract which might cause a disease condition.

AMP as a drug fighting against bacteria

IN 2016 Lam *et al.,* described **SNAPPS**

SNAPPS stands for-
Structurally
Nanoengineered
Antimicrobial
Peptide
Polymer**S**

SNAPPS are a unique class of star shaped AMPs with activity against broad range of Gram negative bacteria.

SNAPPS are built from short chains of lysine and valine,

These peptide arms are conjugated at one end to a core of poly (amidoamine) and each core may be linked to 16-32 arms resulting into a positively charged protein star about 20nm across.

The goal of this project was to replace chemically synthesised SNAPPs with fully synthetic biological fusion proteins.

Criteria for selecting core proteins

The monomer must be expressible in *E.coli.*

The monomer must self-assemble into a homomultimeric complex.

The complex must have size between 4-25 nm.

The complex must have known structure deposited in PDB.

The N- and or C-termini of the monomers should be free.

The set of complexes should be of diverse shapes.

Different antimicrobial peptides and their sources

PEPTIDE	ORIGIN	ACTION
DEFENSIN	***Crassostrea gigas* (oyester)**	Anti-bacterial, anti fungal
ALYTESERIN	***Alytes obstreticans (Toad)***	Anti-bacterial, cytotoxic
ARENSIN	***Pardachirus pavoninus (fish)***	Cytotoxic
PalG1	**Cow rumen**	Anti-bacterial
PONERICINS	***Pachycondyla goeldii***	
CECROPINS	***Hyalophora cecropia (cecropia moth)***	Anti-bacterial
SQUALAMINE	**Deep water sharks**	
NISIN-34aa	***Lactococcus bacteria***	Anti-bacterial
PUROTHIONINE	***Triticumaetivum plant***	Anti-bacterial, cytotoxic
TYROCIDINE		Anti-bacterial, cytotoxic

Resistance to AMPs

1.Substitution modification
2.Acylation of membrane proteins
3.Activation of some proteolytic enzymes and proteins
4.Efflux pump and modification of targets

Fig.1 Substitution modification

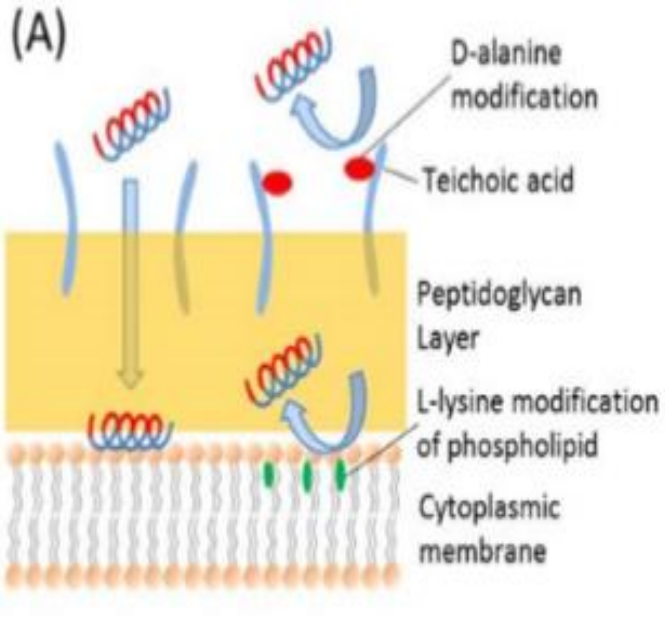


Fig.2 Acylation of membrane proteins

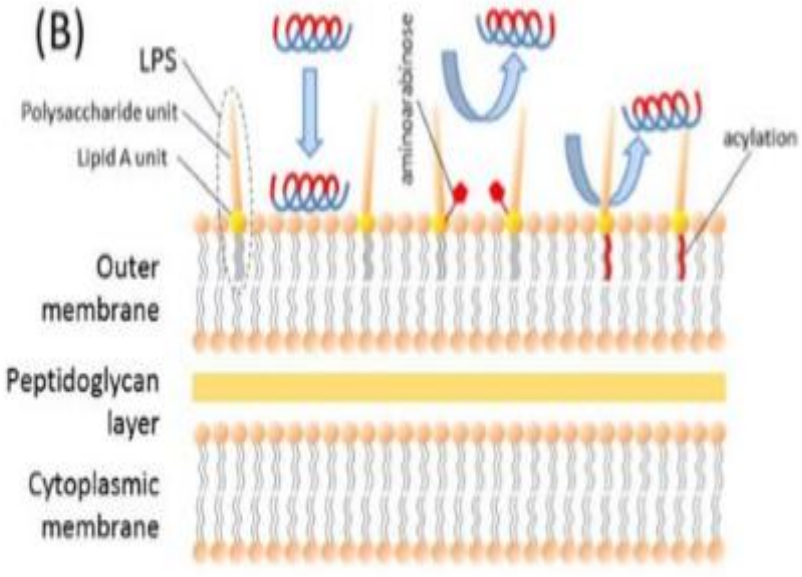
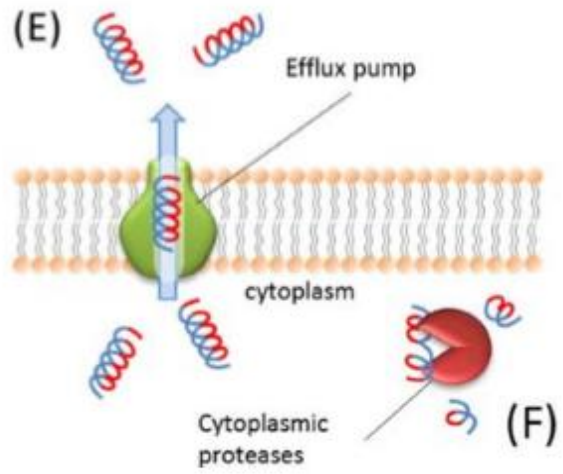


Fig.3 Efflux pump



Conclusion of the study is as follows:

AMPs are multi-purpose and multi-functional peptides with very wide-spectrum use and biological activity.

Based on their natural AMPs, their synthetic analogs can be developed.

They can be used as prebiotic and antibiotics or feed additives to improve the microflora.

Can be developed into synthetic analogs to be used as a mode of treatment against cases of infection with Drug Resistant bacteria as the causative pathogen and can revolutionise treatment protocols all around the world.

References

1. Bonomo, R. A. (2000) Multiple antibiotic resistant bacteria in long-term-care facilities: an emerging problem in the practice of infectious diseases. Clin. Infect. Dis. 31:1414-1422.
2. Brodgen, K.A. (2005): Anti-microbial peptides, pore formers or metabolic inhibitors in bacteria, Nature Reviews Microbiology 3(3): 238-250.
3. Dathe, M and Wieprechet, T (1999) Structural features of helical antimicrobial peptide: their potential to modulate activity on model membranes and biological cells Biochim Biophys Acta. 14(62): 7187.
4. Epand, R. M. and Vogel, H. J (1999) Diversity of antimicrobial peptides and their mechanisms of action Biochim Biophys Acta. 14(62): 11-28.
5. Hotchkiss, R.D. and Dubos, R.J. (1940) Fractionation of the bactericidal agent from cultures of a soil Bacillus. J. Biol. Chem. 132, 791–792.
6. Zasloff, M. (2002) Antimicrobial peptides of multicellular organisms. Nature, 415: 389–395.

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