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A Review on the competence of Defensins to become alternative of antibiotics

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ABSTRACT

Defensins are highly cationic proteins consisting of 20-40 amino acids, having antimicrobial potential. Size of defensins vary between 3 to 5 kDa and are found in human, plants and several subhuman species such as ducks, insects, penguin etc. Because of their antimicrobial efficacy, they boost the immune system. In human alpha and beta-defensins play a pivotal role in providing the first line of defence against microbial infection in several occasions. Plant defensins are small, highly stable and cysteine-rich peptide that constitute a part of the innate immune system against pathogens. Plant defensins also exhibit remarkable antifungal and antibacterial potencies. Till date antibiotics are the mainstay of medical science for the fight against microbial infections. As the disadvantages and limitations of antibiotic use are growing on the hunt for new preventive and therapeutic means is increasing worldwide. To that end, defensins especially plant-based defensins can become a major alternative to antibiotics. In this review, the antimicrobial efficiency of defensins have been thoroughly discussed, and focus has been given to highlight the competence of defensins mainly plant-based defensins as a substitute for antibiotics.

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INTRODUCTION

Defensins are highly cationic proteins of 3-5 kDa in size which are formed by 20 to 40 amino acids. They are diverse members of a large family of antimicrobial peptides, providing antimicrobial action of granulocytes, mucosal host defence in the small intestine and epithelial host defence in the skin and elsewhere (Ganz, 2003). They are antimicrobial and cytotoxic peptides that contain 29-35 amino acid residues including six invariant cysteines which have intramolecular disulfide bond (Lehrer *et al.,* 1993). Plants are sessile organisms that are continuously attacked by fungal pathogens during their life cycle. However, very few pathogen attacks cause the occurrence of full-blown disease (van der Weerden *et al.,* 2013). In plants, defensins are small basic peptides, produced by transcription and translation of a single gene that can be delivered rapidly after infection with an input of energy and biomass (Thomma *et al.,* 2002). Attenuated expression of defensins cause immunity in the host and may alter the balance towards inflammation. The altered productions of defensins contain an integral element in the pathogenesis of inflammatory bowel diseases (Ramasundara *et al.,* 2009). Apart from human defensins are also found in subhuman species such as insects, ducks, penguin etc. Amongst plant species defensins are found in *Spinacia oleracea*, *Elaeis guineensis*, *Dahlia merckii*, *Arabidopsis halleri* etc. (Thomma *et al.,* 2002). Sci-

entists have already reported the antimicrobial activity of defensins. However, as the search for new preventive and therapeutic measure for microbial diseases is on to avoid the menace of rigorous use of antibiotics, a more target specific and validated approach is needed to establish the potential of defensins as an alternative to antibiotics. In this review paper, we have highlighted the efficacy of defensins as antimicrobial agents and discussed the potencies of defensins to replace antibiotics in the future. Moreover, we also conferred about the proficiency of plant-based defensins as antimicrobial agents.

Types of defensin

Six alpha-defensins have been found in humans. Initially, human alpha-defensin peptides were isolated from the neutrophils and are thus called human neutrophil peptides (Bowdish *et al.,* 2006; Nassar *et al.,* 2007) Table 1.

It has been reported that HNP-1,2 and3 are encoded by two genes DEFA1 and DEFA3 localised at chromosome 8, location 8p23.1. DEFA1 and DEFA3 encode identical peptides except for the conversion of the first amino acid from alanine in HNP-1 to aspartic acid in HNP-3; HNP-2 is an N-terminally truncated isoform lacking the first amino acid (Bowdish *et al.,* 2006; Nassar *et al.,* 2007).

These small arginine-rich peptides play important roles in processes related to host defence, being the effectors and regulators of innate immunity as well as enhancers of adaptive immune responses. Four defensins, called neutrophil peptides 1 to 4, are stored primarily in polymorphonuclear leukocytes. Major sites of expression of defensins 5 and 6 are Paneth cells of the small intestine in human (Szyk *et al.,* 2006). The antimicrobial and chemotactic activity of HNP4 is comparable to other human neutrophil defensins. Neither of the intestinal defensins appears to be chemotactic, and for HD6 also an antimicrobial activity has yet to be ob- served. The unusual biological inactivity of HD6 may be associated with its structural properties, making it different from other human alpha-defen- sins. The strongest cationic properties and unique distribution of charged residues on the molecular surface of HD5 may be associated with its highest bactericidal activity among all human alpha-defen- sins (Dhople *et al.,* 2006).

As defensins are a part of the host immune system, they are used in a wide variety of conditions and diseases. In many cases, a disease state is accompanied by a change in the amount of defensin expression in the diseased tissue. Patients having vascular disease show high levels of defensins in atherosclerotic plaques thereby indicating their involvement in vascular diseases. It has been found that defensins interfere with LDL (low-density lip- oprotein, known as "bad cholesterol") and Lp(a) (lipoprotein a) degradation and therefore contrib- ute to the accumulation of these lipoproteins in the body. Defensins also appear to inhibit angiogene- sis, a defect associated with traumatic aortic dis- section and coronary artery disease (García- Olmedo *et al.,* 1998).

Beta-defensins are a family of mammalian defensins mostly found in human, rabbit and guinea-pig etc. These are antimicrobial peptides implicated in the resistance of epithelial surfaces to microbial colonisation. It has been found that beta-defensins, especially human beta-defensin-2 (hβD2), induce the activation and degranulation of mast cells, resulting in the release of histamine and prostaglandin D2 (Bensch *et al.,* 1995). Among the identified human β-defensins, HβD-3 is of special interest for structural and functional studies and possible pharmaceutical applications. It is also one among the identified human defensins which can undergo oligomerisation. Its ability to exhibit antibacterial activity towards Gram-positive bacteria and its involvement in adaptive immunity is of biological significance as compared to other human defensins. The ability to form a dimer that leads to the formation of higher ordered oligomeric structures is possibly responsible for its unique characteristics. These properties of HβD-3 are of current interest and further studies, though a modified analogue of HβD-3 forms only monomeric structures and retain antibacterial activity. It is expected that future studies on this peptide will be directed towards understanding the discrete structural elements that may be responsible for its biological activity and the steps involved in its functional regulation (García-Olmedo *et al.,* 1998).

Apart from alpha and beta-defensins another important defensin type known as theta-defensins (θ-defensins) are a family of mammalian antimicrobial peptides, mostly found in 'Old World' primates, but not in human, gorilla and chimpanzee. These theta defensins are cyclic peptides of 18 amino acids (~2 kDa), consist of a pair of antiparallel β-sheets joined by three disulphide bonds arranged as a ladder to form an extremely stable structure. They possess antimicrobial activity against Gram-positive and Gram-negative bacteria, fungi, and some retroviruses. Additionally, these peptides may self-associate into trimmers (Münk *et al.,* 2003). Theta-defensins have multiple arginines and a ladder-like tri-disulfide array spanning their two antiparallel β-strands. Human θ-defensin genes have a premature stop codon which prevents effective translation of the needed precursors; consequently, these peptides are absent in human leukocytes. Synthetic θ-defensins having

sequences that correspond to those encoded within the human pseudogenes are called retrocyclins. Retrocyclin-1 inhibits the cellular entry of HIV-1, HSV, and influenza A virus. In an experiment, it was shown that rhesus θ-defensin RTD-1 protects mice from severe acute respiratory syndrome coronavirus infection, and retrocyclin-1 protects mice from infection by Bacillus anthracis spores. The small size, unique structure, and multiple host defence activities of θ-defensins make them potential therapeutic agents (Münk *et al.,* 2003).

Table 1: Major Human alpha-defensins

Gene	Aliases/Peptides	Sequence
DEFA1	HNP1 (human neutrophil peptide 1)	ACYCRIPACIAGERRYGTCIYQGRLWAFCC
	HNP2 (human neutrophil peptide 2)	CYCRIPACIAGERRYGTCIYQGRLWAFCC
DEFA3	HNP3 (human neutrophil peptide 3)	DCYCRIPACIAGERRYGTCIYQGRLWAFCC
DEFA4	HNP4 (human neutrophil peptide 4)	VCSCRLVFCRRTELRVGNCLIGGVSFTYCCTRV
DEFA5	HD5 (human defensin 5)	ATCYCRHGRCATRESLSGVCEISGRLYRLCCR
DEFA6	HD6 (human defensin 6)	AFTCHCRRSCYSTEYSYGTCTVMGINHRFCCL

Table 2: Identified plant defensins and their sources

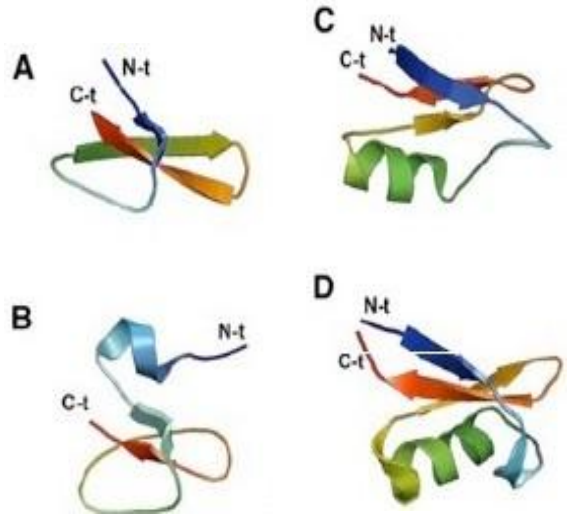
Source	Plant defensins
Flower of *Nicotiana alata*	Nicotiana alata Defensin (NaD1)
Flower of *Nicotiana tabacum* (Common Tobacco)	Flower-specific thionin (FST)
Seeds of Brassicaceae species such as radish, mustard, turnip and *Arabidopsis thaliana*	Antifungal proteins
Sorghum	Inhibitors of insect alpha-amylases
Solanum tuberosum (potato)	Protease inhibitor P322
Vigna unguiculata (Cowpea)	germination-related protein
Sunflower	gamma-thionin (SF18)
Glycine max (Soybean)	sulfur-rich protein SE60
Vicia faba (Broad bean)	fabatin-1 and -2
Endosperm of *Triticum aestivum* (Wheat)	gamma-purothionins
Hordeum vulgare (Barley)	gamma-hordothionins

Plant defensins are a family of small, cysteine-rich proteins found in plants that serve to defend them against parasites (Table 2). These proteins generally consist of about 45 to 50 amino acid residues in their mature form (Bruix *et al.,* 1993; Gu *et al.,* 1992; Terras *et al.,* 1993; Bloch and Richardson, 1991; Ishibashi *et al.,* 1990; Choi *et al.,* 1993) Table 2.

Structural confirmation

The primary structure of defensins includes 45 to 54 amino acid residues with considerable sequence variation. Its three-dimensional structure is small and globular, composed of three antiparallel β-sheets and one α-helix, which is highly conserved among these peptides (de Oliveira Carvalho and Gomes, 2009).

Plant defensins are present as a well-conserved three-dimensional structure made by a cysteine-stabilised α/β (CSαβ) motif, which forms one α-helix and three antiparallel β-sheets. The amino acid sequence is quite conserved, due to the presence of six to eight cysteine residues, which form around three to four disulfide bridges in the sequence of Cys1-Cys8, Cys2-Cys5, Cys3-Cys6, and Cys4-Cys7. Plant defensins having five disulfide bonds have also been described, such as the peptide from *Petunia hybrida* (PhD1), whose cysteine residues interact in the following order: Cys1-Cys10, Cys2-Cys5, Cys3-Cys7, Cys4-Cys8, and Cys6-Cys9. The additional disulfide bond does not affect the typical three-dimensional structure of the defensin, which is located after the α-helix and first β-sheet (Lacerda *et al.,* 2014).



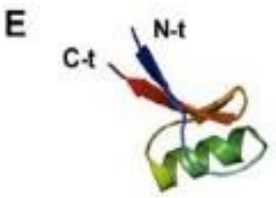


Figure 1: 3D structure of selected members of plant defensin protein superfamily; A. *Petunia hybrid* B. *Raphanussativus*C. *Aesculushippocastanum*D. *Nicotianaalata*E. *Pisumsativum*

Antibiotics, the principal weapon against microbial diseases but with limitations

The introduction of penicillin occurs in 1940. With the growing need because of its capability to ameliorate a plethora of diseases, antibiotics have become the cornerstones of modern medicine. They became the foundation for the treatment of bacterial infections in humans and animals. However, two developments have been occurred to make it more and more difficult to treat against bacterial infection. Firstly, there has been an increasing number of antibiotic-resistant pathogens.

On the other hand, the number of new antibiotics developed (since 1970) has been steadily decreased. According to the estimate of WHO, the worldwide prevalence of antibiotic-resistance is one of the greatest dangers to human health. Without antibiotics, many of the therapies and medical procedures such as chemotherapy, organ transplants, joint operations and the care to premature babies would not be possible (White, 2011). Antibiotics are formed by microorganisms present in the soil and microbes in other habitats. The clusters of the antibiotic-specific gene are located near areas of genes that encode resistance. The genes for antibiotic production and resistance-specific bacteria are often transferred through horizontal gene transfer within bacterial species. The resistance which is selected very often and quick varies greatly between the different bacterial species. Some of the species that are already equipped with intrinsic resistance to many antibiotics acquire new resistance genes very quickly. Because of these multiple-resistant pathogens, the associated diseases are becoming very difficult to treat (Livermore, 2003). More research should be carried out to reduce the spread of resistance and to develop new antibiotics, and the framework conditions are necessary which will allow research discoveries to implement. Antibiotics have several mechanisms of action. Among them, interaction with bacterial cell wall is most common. For example, penicillin-binding proteins (PBPs) are that enzymes which are responsible for the synthesis of the bacterial cell wall, i.e., cross-linking of the peptidoglycan (Mori *et al.,* 1996). The primary PBPs which are inhibited by the carbapenems are high- molecular weight enzymes 1a, 1b, 2 and 3 (Sumita and Fakasawa, 1995). The inhibition of PBP 1a and 1b results in the formation of spheroplasts and rapid killing of bacteria (Curtis *et al.,* 1979). The inhibition of PBP 2 causes the rod-shaped organisms to become spherical and inhibition of PBP 3 results in the formation of filamentous-shaped organisms (Curtis *et al.,* 1979). The binding of PBP with doripenem varies. In the case of *E. coli*, doripenem preferentially binds to PBP 2, followed by the PBP 1a, 1b and 3 (Davies *et al.,* 2008). For *Pseudomonas aeruginosa*, doripenem binds to PBP 2 and 3, followed by PBP 1a and 1b (Davies *et al.,* 2008) whereas, for *Streptococcus pneumonia*, doripenem shows high affinity for PBP 1a, 2b and 2x (Davies *et al.,* 2008).

Disadvantages of antibiotics

The discovery of antibiotics has greatly affected the world in which we live. The overuse of antibiotics is one of the major medical concerns worldwide. It not only contributes to the increase in the bacterial infections but also leads to the development of resistant bacteria to the antibacterial medications (Hayes *et al.,* 1993). Use of antibiotics brings several side effects including malabsorption characterised by a celiac like a syndrome that altered metabolism and overgrowth by some resistant organism (Levy, 2000). Most common side effects that are observed immediately after administration of antibiotics is antibiotic-associated diarrhoea (AAD). Some of the patients develop more severe pathologies that include inflammation of colitis. Another important aspect is sometimes antibiotics show their toxicity on microorganisms that are not the intended targets (Nordberg *et al.,* 2009). These non-target organisms comprise the majority of microbial life that is a natural inhabitant of the human body environment. The therapeutic levels of antibiotics exposed thus cause serious public health hazard (Andersson and Hughes, 2014).

Antimicrobial potencies of defensins similar to antibiotics

Though antibiotics are still major therapeutic measures available for the treatment of most of the human diseases associated with microbial especially bacterial involvement due to noticeable side effects allied with rigorous use of antibiotics, scientists have already started extensive investigations for developing an alternative mode of preventive/therapeutic measures to boost the medical science. Uncontrolled and excessive imprecise use of antibiotics also developed the principle of multidrug resistance (Imran *et al.,* 2017). Use of plant-based defensins can be a new approach towards development of alternative therapy for antibiotics. There are several reports regarding antimicrobial

potencies of human defensins as well as defensins from other sub-human species. To that end, reports have been found that human defensing HBD4 can cause considerable damage to the inner membrane of *E. coli* though it does not kill *E. coli* by a simple mechanism involving membrane permeabilisation (Mathew and Nagaraj, 2017). It has also been found that defensins in retinal Müller glia can phagocytise and kill the bacteria in a time-dependent manner (Singh *et al.,* 2014). Among human defensins, β-defensin family plays a pivotal role in innate immunity. Human β-defensins-2 and -3 (HBD2 and HBD3) show substantial sequence identity and structural similarity. However, HBD3 kills *Staphylococcus aureus* with a 4to 8fold higher efficiency compared to HBD2, whereas their efficacies against *Escherichia coli* are very similar. The generation of six HBD2/HBD3-chimeric molecules helps in the identification of distinct molecular regions which mediate their different killing properties. It has been found that one of the chimaeras (chimaera C3) killed both *E. coli* and *S. aureus* with an even higher efficacy compared to the wild-type molecules. Due to the broad spectrum of its antimicrobial activity against many human multidrug-resistant pathogens, this HBD2/HBD3-chimeric peptide vows for a promising alternative candidate for antibiotics (Spudy *et al.,* 2012). Studies also revealed that HBD-3 was more potent at low concentrations compared to other antibiotics when treated against *Staphylococcus aureus*. Moreover, it has been found that when *S. aureus* biofilm was treated with HBD-3, clindamycin and vancomycin separately, human β-defensin three was significantly more effective against bacteria from the *S. aureus* biofilms than was clindamycin. Vancomycin was not able to reduce the *S. aureus* biofilm area (Huang *et al.,* 2012). There are also reports that human β-defensin2 has a potential therapeutic role against bacterial pathogens and particularly against those exhibiting multidrug-resistant phenotypes (Routsias *et al.,* 2010). Tonsils are believed to play an imperative role during the development of the immune system. Though diseases of the tonsils such as hypertrophy of the tonsil, acute tonsillitis, chronic tonsillitis or peritonsillar abscess are common but very little is known about the underlying pathophysiology and the antimicrobial peptides produced by the tonsils. The human beta-Defensins 1-3 (HBD1-3) are naturally produced having antimicrobial activity against different bacteria, fungi, and viruses. Scientists have studied the concentrations of HBD1-3 in different states of diseases of the tonsillapalatina. They found that in the hyperplastic tonsillapalatina, HBD1-3 play an important role. During tonsillitis mouth constantly faces a high bacterial load. It has been found that HBD1 concentration becomes lower during acute tonsillitis compared to non-acute infected tonsil because HBD1 is being consumed for fighting the bacterial infection (Schwaab *et al.,* 2010). It has been reported that the antimicrobial peptide protegrin-1 (PG-1) inhibit the growth of drug-susceptible and multidrug-resistant *Mycobacterium tuberculosis*; a lower activity has been shown by human beta-defensin-1 (HBD-1) against both strains. The combination of PG-1 or HBD-1 with isoniazid significantly reduced *M. tuberculosis* growth in comparison with the peptides or isoniazid alone (Fattorini *et al.,* 2004). A novel avian beta-defensin (AvBD) has also been found and isolated from duck pancreas. It has been found that AvBD2 is highly expressed in the trachea, crop, heart, bone marrow, and pancreas; moderately expressed in the muscular stomach, small intestine, kidney, spleen, thymus, and bursa of Fabricius; and weakly expressed in skin. Scientists produced and purified recombinant AvBD2 by expressing the gene in *Escherichia coli*. This recombinant peptide exhibited strong bactericidal properties against *Bacillus cereus*, *Staphylococcus aureus*, and *Pasteurella multocida*, and weak bactericidal properties against *E. coli* and *Salmonella choleraesuis*. Moreover, this recombinant protein retained antimicrobial activity against *S. aureus* under different temperatures ranging from -20 degrees C to 100 degrees C and pH values ranging from 3 to 12 (Ma *et al.,* 2009). Scientists also have isolated spheniscin, a beta-defensin from the penguin stomach. Studies also geared up the expectation of development of interesting probes from penguin defensins for the designing of highly efficient antibiotics to fight off pathogens that develop in relatively salt-rich body fluids (Landon *et al.,* 2004). Apart from duck, penguin and insects, beta-defensins has also been derived from chicken bone marrow amongst sub-human species which is also capable of showing its antibacterial activity (Derache *et al.,* 2009).

Antimicrobial activities of plant defensins

Antifungal

Biotechnologists use antifungal peptide genes to generate important agronomical traits resistant to fungal disease. The first study which was attempted to highlight this class of plant antifungal defensins was carried out with two peptides, isolated from radish seeds, Rs-AFP1 and Rs-AFP2. Both peptides were assayed against 20 different plant pathogenic fungi, and the lower protein concentration required for 50% inhibition of fungal growth (IC_{50}) was obtained by Rs-AFP2 when assayed against *Pyricularia oryzae.* $IC_{50}$was found to be between 0.08 to 5 μM. The defensins were reported having high biological activity containing a range of micromolar to nanomolar. The im-

portance of disulfide bonds in defensins stabilisation and the role of inorganic ions in its antifungal activity have already reported (Lacerda *et al.,* 2014).

Antibacterial

Plant antibacterial peptides are of great importance as components of barrier defence induced upon infection in a wide variety of plants. They have been isolated from a wide variety of species. They consist of several protein groups having different features, such as the overall charge of the molecule, the content of disulphide bonds, and structural stability under environmental stress (De Caleya *et al.,* 1972). The first antibacterial peptide which was isolated from plant species was purothionin from wheat flour (*Triticum aestivum*), which can inhibit the growth of phytopathogens such as *Pseudomonas solanacearum*, *Corynebacterium michiganense* etc. The antibacterial peptides have been isolated from roots, seeds, flowers, stems, and leaves of different plant species and demonstrated the activity towards phytopathogens, as well as against bacteria which is pathogenic to humans (Barbosa Pelegrini *et al.,* 2011).

Other beneficial actions of plant defensins

Apart from its antibacterial and antifungal activities plant defensins also exhibit several other potentially beneficial actions. Defensins and other related defence proteins present in legumes show HIV-1 reverse transcriptase inhibitory activity and antitumor activities (B Ng *et al.,* 2011). It has also been found that in *Medicago truncatula*, nodule-specific cysteine-rich (NCR) peptides inhibit pathogen growth and collectively act as plant effectors inducing irreversible differentiation of rhizobia to nitrogen-fixing bacteroids (Maróti *et al.,* 2015). Moreover, it has also been reported that plant defensin AhPDF1.1b exhibits an unexpected role by conferring zinc tolerance to yeast and plant cells. It has been found that plant defence AhPDF1.1b which is already known for its antifungal activity also shows its potential as a beneficial factor involved in adaptive response to zinc overload when it is expressed in yeast cells (Mith *et al.,* 2015).

Mechanism of action of defensins

From the available reports so far, it is clear that defensin peptides are involved in plant defence (Selitrennikoff, 2001). Their distribution is consistent with their role of putative defence. They are mostly identified in leaves, tubers, flowers and seeds, which plays an important role in the protection of germinating seeds and developing seedlings (García-Olmedo *et al.,* 1998).

The transcripts of most of the plant defensins can be divided into two major classes. The first and largest class is the precursor protein that is composed of an amino-signal peptide that targets the peptide to the extracellular space. The second class of defensins is produced as a larger precursor with C-terminal prodomains (Stotz *et al.,* 2009).

Few hypotheses try to explain the mechanism of action of antimicrobial defensins. The main hypothesis for their mechanism of action involves the ability of AMPs to collapse the membrane by interacting with molecules of lipid on the bacterial cell surface. According to this hypothesis, the cationic peptides are attracted electrostatically to negatively charged molecules such as anionic phospholipids, lipopolysaccharides (LPS) (Gram-negative) and teichoic acid (Gram-positive), which are located asymmetrically in the membrane. The positively charged residues also interact with the membrane lipids through specific receptors at the surface of the cell. Consequently, peptide binds to the membrane that activates several pathways that will cause cell death (Yeaman and Yount, 2003).

However, one general mechanism of action for antibacterial peptides is observed in most peptides. When they reach the threshold concentration, cationic peptides accumulate on the surface of the membrane in order to direct inner targets for cell lysis. The intrinsic and extrinsic parameters have been reported to influence the threshold peptide concentration. Intrinsic factors have the ability of peptides to self-assemble and oligomerize, while extrinsic determinants include the composition of the membrane phospholipids, membrane fluidity and size of the head group. These factors influence the membrane potential, which is critical for determining the threshold peptide concentration (Broekaert *et al.,* 1997).

The barrel-stave mechanism consists of the peptides which aggregate and forms a barrel-ring around an aqueous pore. Peptides interact with the membrane, forcing one thin and hydrophobic portion to bind with the phospholipid acyl-chains. After reaching to the threshold concentration, peptides from the barrel-ring open a pore in the membrane. Their hydrophilic portion comprises the core of the barrel, while the hydrophobic portion interacts with the membrane phospholipids of bacteria (Broekaert *et al.,* 1997).

The toroidal pore or wormhole hypothesis also proposes the formation of pores in a barrel-stave shape. However, these pores are composed of overlapping peptides and membrane lipids, generating supermolecular complex. In this structure, the transmembrane pore is formed by the peptide and phospholipid head group. Therefore, the displacement of polar head groups from the peptides

induces strains of positive curvature in the membrane by breaching the hydrophobic region (Yeaman and Yount, 2003).

In the carpet mechanism, initially, the peptides are present in the monomeric or oligomeric form that electrostatically binds to the cell surface, covering all the membrane and giving an appearance of a peptide carpet on the bacterial membrane surface. Consequently, the carpet causes a phospholipid displacement that alters the fluidity of the membrane and reduces the barrier properties of the membrane. It also leads to disruption of the membrane and, further cell death. Due to the unfavourable energy which is observed after the membrane bilayer becomes curved, the cell was rupturing, and cell lysis will occur. In this process, the membrane damage occurs in a dispersion-like manner without any formation of a channel (Papo and Shai, 2003).

Plant-based defensins are becoming the major target of investigations for the development of new antimicrobial drugs to replace antibiotics. Scientists have already isolated defensins from potato, sunflower, peas, wheat, soybean etc. (Table 2). From the Indian context, the novel antibacterial peptide has already been isolated from curry leaves (Imran, 2013) which are one of the major ingredients of many food dishes across this subcontinent. Though, more research is needed in this field to develop validated antimicrobial drugs from plant defensins.

CONCLUSION

In this review paper, a discussion has been made on defensins, their types, structure, properties and mechanism of action. Antimicrobial capabilities of defensins found in human and other subhuman species have also been discussed. Moreover, the efficacy of plant defensins is also highlighted focusing on their antibacterial and antifungal actions. These highly cationic proteins act as the first line of defence against potential bacterial and fungal pathogens. The discovery of antibiotics was a crucial step in medical science. Till date, they are the foundation for the treatment of bacterial infections in human beings as well as animals, but the dreadful side of antibiotic is that they cause many side effects such as nausea, headache, diarrhoea, malabsorption etc. Moreover, overuse of antibiotics is associated with the development of multi-drug resistant strains of microbes. Thus, defensins, mainly plant-based defensins can become the prime target for drug development for the treatment of various pathogenic diseases with lesser side effects.

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