



## Antimicrobial Peptides: The Possible Solution for Antibiotic Resistance against Phytopathogens

(Manasa C.<sup>1</sup> and \*Anusha Nitta<sup>2</sup>)

<sup>1</sup>College of Horticulture, Bengaluru, University of Horticultural Sciences, Bagalkot- 560065, Bengaluru

<sup>2</sup>Division of Entomology, Tamil Nadu Agricultural University, Coimbatore - 641003, Tamil Nadu, India

\*Corresponding Author's email: [anushanitta2@gmail.com](mailto:anushanitta2@gmail.com)

Agriculture and its allied sectors remain to be a key component for global food security. The intensified cropping pattern has exposed the plants to various biotic and abiotic stresses. Among the biotic stress, phytopathogens are considered to be one of the significant factor in reducing the production and productivity. The plant disease has resulted in annual estimated loss of 10–15% of the world's major crops, with direct economic losses of up to hundreds of billions of dollars (Chatterjee *et al.*, 2016). The success of antibiotics against pathogens in due course of time soon resulted in the employment of molecule to the management of the phytopathogens. Unfortunately, the erratic usage pattern of these antibiotics has aroused the resistance phenomena in pathogens resulting in failure of the molecules. Apart from the usage pattern, only few antibiotics registered against the phytopathogens has boosted up the development of resistance in plant pathogens. The current scenario has resulted emergency ringtones for the novel compounds that could be hard enough for the super bugs to develop resistance. The intense exploration of the natural products by the scientific community has bobbed up with novel molecule called Antimicrobial Peptides (AMPs).

### Brief note on AMPs

The AMPs are 12 to 50 amino acid short polypeptide molecules that are universally produced in all living organisms as a defense strategy (Magana *et al.*, 2020). These molecules possess broad-spectrum activity against multiple classes of bacteria, fungi, virus, yeast and parasites displaying bacteriostatic, microbicidal and cytolytic properties (Huan *et al.*, 2020). In general, these peptides are positively charged and are accompanied by 40 or 50 per cent of hydrophobic amino acids (Nguyen *et al.*, 2011). The presence of both hydrophilic and hydrophobic amino acids results in the formation of the amphipathic structure enabling them to the interact with the pathogens followed by permeabilizing the bacterial membrane and resulting in causing unbalanced ion flow leading to membrane depolarization. Additionally, the peptides have showed additional or complementary mechanisms like targeting intracellular process vital for the cellular physiology such as protein, DNA, RNA, Enzyme synthesis inhibition, blocking of chaperone necessary for protein folding, Inhibition of cellular respiration and induction of Reactive Oxygen Species (ROS) formation, disruption of mitochondrial cell membrane integrity *etc* (Harris *et al.*, 2009). Further, its speed of action and low propensity for the development of the resistance highlights AMPs as a potential candidate against antibiotics (Bradshaw, 2003).

## Successful attempts of AMPs against phytopathogens

Several laboratory studies have been carried out in order to assess the efficacy of the AMPs against phytopathogens. The below mentioned examples prove the potentiality of the molecule. Assessment of RW-BP100 has registered 55-67 per cent of inhibition at 25  $\mu$ M concentration along with half maximal inhibitory concentration (IC<sub>50</sub>) ranging from 3-3.7  $\mu$ M (Mendes *et al.*, 2021). MSI-99, a derivative of the magainin has displayed significant inhibition of multiple bacterial and fungal species. *viz.*, *Pseudomonas spp.*, *Xanthomonas campestris* pv. *vesicatoria*, *Clavibacter michiganensis* subsp. *michiganensis*, *E. carotovora* subsp. *carotovora*, *E. carotovora* subsp. *chrysanthemi*, *Agrobacterium tumefaciens*, *Penicillium digitatum*, *Alternaria solani*, *Phytophthora infestans* with MIC ranging from 5-10  $\mu$ g/ml (Alan and Earle, 2002). BP100 analogs, displayed an infection reduction of 95-10 per cent of *X. axonopodis* pv. *vesicatoria* and *P. syringae* pv. *syringae* in pepper, pear leaves and immature fruits of pear (Guell *et al.*, 2012). Further, the heterologous expression of Cecropin A and B in rice confer protection against *Magnaporthe grisea* (Coca *et al.*, 2004) and *Xanthomonas oryzae* (Sharma *et al.*, 2000).

The AMPs also work as systemic defense inducer in plants apart from the direct efficacy of the molecule against pathogens.

## Cytotoxic effect and Phytotoxicity of AMPs

Apart from the efficacy of the AMP against phytopathogens, its toxicity towards the plants defines the safety for its exploitation. The works in this aspect has proved that these molecules cause negligible toxicity to the plants even at higher concentrations. For example, Tobacco protoplasts displayed no visible effects of cell division and viability upon treatment with CEMA (Cecropin A- melittin hybrid) at a threshold concentration of 30  $\mu$ g/ml (Yevtushenko *et al.*, 2005). Pollen germination assay of kiwifruit displayed an inhibition of both pollen germination and tube elongation upon treatment with Magainin 1 and 2 realizing the ill effect of peptide in the plant system (Jacobi *et al.*, 2000). Peptide and its derivatives set forth expression of lesions in tobacco leaves and affected rice seedling development at 16-32  $\mu$ M (Nadal *et al.*, 2012).

Hence, the efficacy of AMPs towards the phytopathogens and its safety towards the plants suggests that prominence of the molecule in combating the phytopathogens and its resistance towards antibiotics.

## References

1. Coca M, Penas G, Gomez J ´ et al. (2006) Enhanced resistance to the rice blast fungus *Magnaporthe grisea* conferred by expression of a cecropin A gene in transgenic rice. *Planta* 223: 392–406.
2. Sharma A, Sharma R, Imamura M, Yamakawa M & Machii H (2000) Transgenic expression of cecropin B, an antibacterial peptide from *Bombyx mori*, confers enhanced resistance to bacterial leaf blight in rice. *FEBS Letters* 484: 7–11.
3. Chatterjee S., Kuang Y., Splivallo R., Chatterjee P., Karlovsky P. (2016). Interactions among filamentous fungi *Aspergillus niger*, *Fusarium verticillioides* and *Clonostachys rosea*: fungal biomass, diversity of secreted metabolites and fumonisin production. *BMC Microbiol.* 16, 83–83
4. Magana, M., Pushpanathan, M., Santos, A. L., Leanse, L., Fernandez, M., Ioannidis, A., Giulianotti, M. A., Apidianakis, Y., Bradfute, S., Ferguson, A. L., Cherkasov, A., Seleem, M. N., Pinilla, C., de la Fuente-Nunez, C., Lazaridis, T., Dai, T., Houghten, R. A., Hancock R. E. W. and Tegos, G. P., The value of antimicrobial peptides in the age of resistance. *Lancet Infect Dis.*, 20(9): 216-230.
5. Nguyen, L. T., Haney, E. F. and Vogel, H. J., 2011, The expanding scope of antimicrobial peptide structures and their modes of action. *Trends Biotechnol.*, 29: 464–472.

6. Harris, M., Mora-Montes, H. M., Gow, N. A. and Coote, P. J., 2009, Loss of mannosylphosphate from *Candida albicans* cell wall proteins results in enhanced resistance to the inhibitory effect of a cationic antimicrobial peptide via reduced peptide binding to the cell surface. *Microbiol.*, 155: 1058–1070.
7. Bradshaw, J. P., 2003, Cationic antimicrobial peptides: issues for potential clinical use. *BioDrugs*, 17: 233-240.
8. Mendes, R. J., Regalado, L., Luz, J. P., Tassi, N., Teixeira, C., Gomes, P., Tavares, F. and Santos, C., 2021, *In Vitro* Evaluation of Five Antimicrobial Peptides against the Plant Pathogen *Erwinia amylovora*. *Biomol.* 11(4): 554.
9. Alan, A. R. and Earle, E., 2002, Sensitivity of bacterial and fungal plant pathogens to the lytic peptides, MSI-99, magainin II, and cecropin B. *Mol. Plant-Microbe Interact.*, 15: 701–708.
10. Guell, I., Ferre, R., Kasper, K. Sorensen, Badosa, E., Ng-Choi, I., Montesinos, E., Bardaji, E., Feliu, L., Jesen, K. J. and Planas, M., 2012, Multivalent display of the antimicrobial peptides BP100 and BP143. *Beilstein J. Org. Chem.*, 8: 2106–2117
11. Jacobi, V., Plourde, A., Charest, P. J. and Hamelin, R.C., 2000, *In vitro* toxicity of natural and designed peptides to tree pathogens and pollen. *Can. J. Bot.*, 78: 455–461.
12. Nadal, A., Montero, M., Company, N., Badosa, E., Messeguer, J., Montesinos, L., Montesinos, E. and Pla, M., 2012, Constitutive expression of transgenes encoding derivatives of the synthetic antimicrobial peptide BP100: impact on rice host plant fitness. *BMC Pl. Biol.*, 12: 159
13. Yevtushenko, D. P., Romero, R., Forward, B. S., Hancock, R. E., Kay, W. W. and Misra, S., 2005, Pathogen-induced expression of a cecropin A-melittin antimicrobial peptide gene confers antifungal resistance in transgenic tobacco. *J. Exp. Bot.*, 56 (416): 1685- 1695.