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Commentary on Antimicrobial Keratitis

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Commentary

Microbial keratitis is a leading cause of blindness worldwide and results in unilateral vision loss in an estimated 2 million people per year. Bacteria and fungus are two main etiological agents that cause corneal ulcers. Although antibiotics and antifungals are commonly used to treat corneal infections, a clear trend with increasing resistance to these antimicrobials is emerging at rapid pace. Extensive research is carried out to determine alternative therapeutic interventions and antimicrobial peptides (AMPs) are increasingly recognised for their clinical potential in treating infections.

Small molecules targeted against virulence factors of the pathogens and natural compounds are also explored to meet the challenges and growing demand for therapeutic agents. Here we review the potential of AMPs, small molecules and natural compounds as alternative therapeutic interventions for treatment of corneal infections to combat antimicrobial resistance.

Additionally, we have also discussed about the different formats of drug delivery systems for optimal administration of drugs to treat microbial keratitis. Rapid rise of antimicrobial resistance against conventional antimicrobials, resurgence of multidrug resistant microbes and the slowdown in the development of new classes of antimicrobials, necessitates the urgent development of alternate classes of therapeutic molecules. Antimicrobial peptides (AMPs) are small proteins present in different lifeforms in nature that provide defense against microbial infections. They have been effective components of the host defense system for a very long time.

The fact that the development of resistance by the microbes against the AMPs is relatively slower or delayed compared to that against the conventional antibiotics, makes them prospective alternative therapeutics of the future. Several thousands of AMPs have been isolated from various natural sources like microorganisms, plants, insects, crustaceans, animals, humans, etc. to date. However, only a few of them have been translated commercially to the market so far.

This is because of some inherent drawbacks of the naturally obtained AMPs like 1) short half-life owing to the susceptibility to protease degradation, 2) inactivity at physiological salt concentrations, 3) cytotoxicity to host cells, 4) lack of appropriate strategies for sustained and targeted delivery of the AMPs. This has led to a surge of interest in the development of synthetic AMPs which would retain or improve the antimicrobial potency along with circumventing the disadvantages of the natural analogs. The development of synthetic AMPs is inspired by natural designs and sequences and strengthened by the fusion with various synthetic elements. Generation of the synthetic designs are based on various strategies like sequence truncation, mutation, cyclization and introduction of unnatural amino acids and synthons.

In this article, we have described some of the AMPs isolated from the vast repertoire of natural sources, and subsequently described the various synthetic designs that have been developed based on the templates of natural AMPs or from de novo design to make commercially viable therapeutics of the future. This review entails the journey of the AMPs from their natural sources to the laboratory.

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