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Opinion Article

Note on Pulmonary Surfactant and Drug Bioavailability

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ABOUT THE STUDY

This study assesses the relationship between Pulmonary Surfactant (PS) and Antimicrobial Peptides (AMPs) to determine whether PS can transport AMPs and the degree to which PS impairs AMP function and vice versa. This in turn is driven by the requirement to develop fresh methods for treating bacterial infections in the airways. Together with the issue of Multidrug-Resistant (MDR) bacteria, Low Respiratory Tract Infections (LRTIs) are a major cause of illness and death around the world. This highlights the need for effective therapies that guarantee high bioavailability of the drug at the site of infection and display a potent antimicrobial effect. With the hydrophobically end-tagged AMP GRR10W4 (GRRPRPRPWWWW-NH2), which has previously been shown to have significant antimicrobial activity against a wide range of bacteria under varied conditions, we now suggest the combination of AMPs with PS to increase their delivery. Surface balances and bubble surfactometry based experiments with model systems simulating the respiratory interface and an active alveolus were used to show that a fluorescently labeled version of GRR10W4 (GRR10W4-F) was able to interact with and insert into PS membranes without impairing its biophysical function.

As a result, vehiculization of the peptide at air-liquid interfaces was made possible, even at interfaces where surfactant layers had previously been present. Additionally, after GRR10W4-F was delivered, breathing-like compression-expansion dynamics encouraged the interfacial release of the peptide, which may have helped it carry out its antibacterial action. Compared to the peptide alone, PS/GRR10W4-F formulations had stronger antibacterial activity and decreased toxicity on cultivated airway epithelial cells. When considered as a whole, these findings pave the way for the creation of innovative AMP delivery methods that will boost the bioavailability of these molecules at the infection site when used in inhalation treatments. One of the most significant developments in medicine is likely the discovery of antibiotics. Since Alexander Fleming discovered penicillin in 1928, fewer people have died from illnesses as a direct result of the creation and application of antimicrobial substances. Antibiotic abuse and overuse, on the other hand, have resulted in the emergence of Multidrug Resistant (MDR) bacteria, a public health issue that kills hundreds of thousands of people worldwide each year.

AMPs are small amphiphilic molecules that are roughly 10 to 50 amino acids long with a net positive charge of generally +2 to +9 and a high proportion of hydrophobic residues (30%-50%). AMPs have been identified as an important component of the innate immune system in all living organisms, where they form a first line of defense against invading pathogens. These characteristics provide these peptides the ability to interact with and insert into negatively charged bacterial membranes, breaking the lipid membrane-imposed permeability barrier or impeding essential biosynthetic activities. In addition to being active against a broad spectrum of bacteria, AMPs have anti-biofilm functions and play a role in regulating wound healing and the inflammatory response to infection. Despite the extensive *in vitro* activity and potency of many of the recently discovered AMPs, only five are currently approved for clinical use, making these peptides unsuitable for clinical use. The focus is on overcoming the limitations of using it. One of the reasons AMPs fail in clinical trials is their low bioavailability at sites of infection. This is directly related to the method of administration. This is a particular challenge in treating Lower Respiratory Tract Infections (LRTIs), a leading cause of death and disability due to the highly stratified structure of the lungs, along with alveolar collapse caused by infection.

For delivery to the airways, Pulmonary Surfactant (PS) transports the pulmonary barrier (branched structures of the respiratory system, ciliated cells, mucus, correct PS, and the presence of immune cells) and drugs to the distal airways. PS is a lipoprotein substance synthesized by type II alveolar cells and secreted into the alveolar space to minimize surface tension, thereby avoiding alveolar collapse and minimizing the work of breathing. PS is composed primarily of lipids (90% of mass) and a significant proportion (10%) of four specific lung surfactant proteins. A key feature that makes PS attractive as a drug vehicle is its ability to incorporate hydrophobic drugs and diffuse rapidly and efficiently across large air-liquid interfaces.

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CONCLUSION

It has previously been used to deliver various types of drugs that target airway surfaces. Based on this idea, we propose using PS as a vehicle for AMPs to enhance interfacial delivery to the site of infection in pulmonary infections. A combination of AMP and PS as a delivery system has been proposed and evaluated in previous studies. However, to our knowledge, no previous studies have addressed the use of peptides end-labeled with hydrophobic stretches. Peptides are retained. This includes gram-positive bacteria (*Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) bacteria involved in lower respiratory tract infections.