Short Anti-Microbial Peptide Surrogates as Antiseptic Agent to Increase Hygiene in Public Installations

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Challenge

Increasing resistance of microbial, yeast and fungal strains to antibiotic and antifungal treatment is a dangerous trend of last decade. Decreasing efficiency of common treatments poses serious health and economical problem worldwide. Hospitals are a source of microbes due to insufficient hygiene measures [1]. Recently, we have isolated and characterized remarkable antimicrobial peptides (AMPs) surrogates [2-5] which mechanism of action promises robust solution is preventing further development of resistance. The peptide surrogates suggested are nontoxic. Very effective broad-spectrum antimicrobials, easy and inexpensive to access and formulate and are handled in aerosol or in water solution suitable to keep high hygiene [6-8] at home, in hospitals and public installations like lavatories. We suggest the addition of the AMP surrogates to the list of chemicals applied for sterilization and disinfection of surgical tools as well as cleaning solutions [9,10]. Currently applied antiseptic and sterilizing agents (triclosan, triclocarban, and chloroxylenol) are banned [11], and the pathogenic bacteria are not eradicated. The spread of nosocomial infections is certain [12,13].

Figure 1: Typical bacteria and aerosol with disinfectant [14].

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The antibiotics crisis is suffering, due to resistance to nowadays applied antibiotics [15], and is reflected in the explosive proliferation of killer bacteria and persister [16] cell bacteria at the hospitals. People are getting infected while being treated at hospitals in the various departments with all kinds of bacterial infections; the worse is based on Gram-negative microbes. The incurable diseases are being transferred to the patients from the hospital walls, lavatories, and floors, the hygiene of the medicinal staff and visitors for example.

Figure 2: A nosocomial infection is any infection that is acquired during a stay in a hospital, nursing home, or other healthcare facility. About 5-15% of all hospitalized patients acquire nosocomial infections. Three factors contribute to nosocomial infections: 1) Microorganisms in the hospital. 2) A compromised host. 3) The chain of transmission.

The quest for antibiotics for internal human consumption require according to the FDA regulation progress at a slow, responsible pace. However, Disinfection of the hospital facilities and sterilizations can be carried out with agents that are less toxic to humans but may be very effective in the hygiene area. The novel antiseptic agent can become very useful in the combat of bacteria at hospitals for example. Such agent can involve the application of very potent broad-spectrum bactericides based on antimicrobial peptide surrogates. Such agents should be economic and involve available building blocks allowing large-scale preparation [17], safe application and very effective eradication of bacteria.

Bacteria we expect to find include *E. coli*, *S. aureus*, *Streptococcus*, *Campylobacter*, and *Salmonella* [18]. The measures today use also expects standard household cleaners such as Lysol to be sufficient disinfectants. The alarming situation in the hospitals reveals that this is not enough. The bacteria flourish and ignore currently applied the bactericides applied.

The study is far from the first to examine bugs in bathrooms, but most previous studies looked at specific bacterial species, while the new work looked at whole bacteria communities, said study researcher Noah Fierer, an assistant professor at the University of Colorado.

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Bacteria can be defined as Microorganisms that lack a nucleus and have a cell wall composed of peptidoglycan, a protein-sugar molecule. They are the most common organisms on Earth and are intimately connected to the lives of all organisms (Bacteria, Encarta Online).

Figure 3 shows the basic structure of a typical bacterium cell. We all have been taught the basics about bacteria in lower level sciences, so the point to focus on in our experiment is that they are found everywhere.

Since their discovery in the early 1980s, antimicrobial peptides (AMPs, also called host defense peptides) have stimulated interest as prospective antibiotic agents because they rapidly inactivate a wide range of microorganisms including Gram-positive and negative bacteria, fungi, and some viruses. In many cases, they are indifferent to current multidrug-resistant (MDR) strains [19,20]. Naturally occurring AMPs span a wide range of size, sequence, and structure [21]. They share only amphipilicity and positive charge [22].

The natural products antimicrobial peptides (AMPs) and their synthetic surrogates are essential components of the defense system spanning virtually every kingdom of life. The peptides are relatively small, amphipathic molecules of variable length, sequence, charge, and structure. AMPs have been shown to possess activity against a wide range of microorganisms, including bacteria and fungi, and kill their targets by multiple mechanisms mostly through membrane disruption. The motifs on which bioactivity relies have been identified and mimics of the motifs have been prepared and proven to have the same biological activity as the natural AMP.

The field of AMPs has lately received increased attention, much due to the serious issue of resistance development of microorganism strains against current antibiotics. However, because of the extensive range of microorganism related problems. AMP and modified AMPs were examined with. The field of AMPs is also of interest in other areas such as hygiene applications, which is the main focus of this paper. The use of AMPs especially their synthetic surrogates in hygiene products [6] could prevent common pathogen related problems involved in hygiene. Conditions such as fungal and bacterial infections are related to diapers and panty liners. Also, it is of importance to keep skin and surfaces hygienically. The suggested AMP surrogate’s applications in hygiene products are potentially a useful family of the agent to combat the spread of incurable diseases.

**Bacterial resistance**

Avoiding infection has always been expensive. Some human population escaped tropical infections by migrating into cold climates but then had to procure fuel, warm clothing, durable housing, and crops from a short growing season. Waterborne infections were averted by owning your well or supporting a community reservoir. Everyone got vaccines in rich countries, while people in others got them later if at all.

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Antimicrobial agents seemed at first to be an exception. They did not need to be delivered through a cold chain and to everyone, as vaccines did. They had to be given only to infected patients and often then as relatively cheap injectables or pills off a shelf for only a few days to get astonishing cures. Antimicrobials not only were better than most other innovations but also reached more of the world’s people sooner.

The problem appeared later. After each new antimicrobial became widely used, genes expressing resistance to it began to emerge and spread through bacterial populations. Patients infected with bacteria expressing such resistance genes then failed treatment and remained infected or died. Growing resistance to antimicrobial agents began to take away more and more of the cures that the agents had brought. It then proved to be much more resource-intensive to keep patients from becoming infected with and failing treatment for drug-resistant bacteria than it had been to deliver the drugs that had caused the problem.

Resource-limited countries that had managed to make antimicrobials available to their infected patients could not afford to do all the things that were then needed to manage the antimicrobial resistance that resulted. Antimicrobial resistance seems a function of how many bacteria have been exposed to antimicrobials, for example, so treat only infections that antimicrobials cure for as long, but only as long, as needed. Treating an infecting germ with a drug it resists not only fails but also makes that resistant germ spread, so treat only with the drug that can still kill it. Resistant germs spread to others, so identify them and interrupt their spread. Each of these ways to control resistance costs much more than it had cost to distribute the boxes of pills and injectables that had began the resistance. Expensive microbiology laboratories in rich countries test whether the germ v infecting any patient is of a kind that antimicrobial agents kill, and if so which agent could still kill it. Those countries then make that agent promptly available by keeping ubiquitous costly stocks of all agents.

Rational

Antibiotics have long been used for treating a variety of diseases in humans. They are very useful as drugs because they can kill off the disease-causing organisms without producing harmful side effects in patients. Over recent years, however, many of these drugs have become less effective, and in some cases are now totally useless. The reason for this is that the disease-causing organisms infections have developed a resistance to the drugs which means quite simply that they have found ways to avoid the drugs’ toxic effects. This alarming rise in infections due to drug-resistant bacteria - like MRSA (Methicillin-resistant Staphylococcus aureus) - has given rise to growing public concern, and has prompted a call for new antibiotics that can be used to treat patients infected with the drug-resistant organisms. To trust to luck and hope for some chance discovery of a new drug (as with Fleming’s discovery of penicillin, for example) is not satisfactory: the problem of resistance is with us in the clinics now and must be dealt with more speedily. A more sensible way forward is to design new drugs that work in novel ways, and one such class of compounds that might be exploited are the family of anti-bacterial peptides and anti-bacteria surrogates. In this LOI we would like to apply this modern approach and start with eradicating the stubborn bacteria nesting in the hospitals and facilities. This will demand the verification of items 1 - 4 above applying a suitable budget. It is hoped to pave the way for others to design new and improved forms of antibiotic for use against antibiotic-resistant bacterial infections.

In this letter, we would like to suggest the application of easily accessible short mimics of very potent surrogates of a short motif found in antimicrobial peptides from the skin of the tropical frog Phyllomedusa sauvagii [25]. Despite the growing interest in the use of cationic antimicrobial peptides (AMPs), as a potential source of novel antibiotics, there are but rare instances of rational designs of highly potent and selective AMP analogs that can be manufactured as antibiotics at competitive costs for therapeutic use [19,26-30]. However, recently we have published the application of the 5-amino acid KAAAK motif found in Dermaseptin [31] for the synthesis and biological application for the eradication of broad spectrum of bacteria where 1,4 dihydropyridine 3 and benzodiazepine 4 serve as scaffolds (Figure 1) namely Gram-negative (E. Coli) as well as Gram-positive (Staph. Aureus) at sub micro molar concentrations without substantial toxicity as well as hemolysis no human red blood cells (< 3%) as depicted in the figure 4.

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Now we face a new situation that if not handled properly, may evolve to a world catastrophe for mankind and animals everywhere on planet earth.

<table>
<thead>
<tr>
<th>#</th>
<th>Bacterium</th>
<th>Gram</th>
<th>MIC (Molar concentration) (Full Disappearance) RBC Hemolysis &lt; 3%</th>
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<tbody>
<tr>
<td>1</td>
<td>Coli</td>
<td>Negative</td>
<td>25 x 10^{-8}</td>
</tr>
<tr>
<td>2</td>
<td>Staph aureus</td>
<td>Positive</td>
<td>10 x 10^{-8}</td>
</tr>
</tbody>
</table>

**Table 1: Biological activities of surrogates**

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14. Bacteria are named depending on their shape and arrangement.


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