Natural Antibacterial Surfaces

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In nature, many organisms have evolved a myriad of surfaces with specific physicochemical properties to combat bacteria in diverse environments.

Keywords: natural antibacterial ; surface bacterial fouling

1. Introduction

Manifesting a typical size at least ten orders of magnitude smaller than human beings, bacteria present in various environments and are important to the human being, and ecosystem. Most bacteria are harmless to us, help our bodies digest food and absorb nutrients, and even produce multivitamins in the gut [1]. However, some diseases caused by pathogenic bacteria, such as tuberculosis, pneumonia, endocarditis, sepsis, and osteomyelitis, invade the host and cause various infectious diseases [2][3][4]. Additionally, bacteria such as methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* are well known to trigger surgical site infections through the incision, which threatens millions of patients every year and induces the spread of antibiotic resistance all around the world [5][6]. According to the Centers for Disease Control and Prevention of the United States, antibiotic-resistant bacteria may result in at least 70,000 deaths worldwide per year. By 2050, this number will exceed 10 million [7].

Mitigating or even preventing bacterial infection has been a historic challenge. In ancient times, many natural agents such as herbs, honey, animal feces, and moldy bread have been widely used for treating patients with bacterial infections. Among these, the most effective and widespread agent was moldy bread, although its mechanisms were not clear at that time [8]. Meanwhile, many metals, e.g., copper and silver and their alloys, were also utilized to disinfect wounds and drinking water [9]. The discovery of penicillin was a milestone in the fight against bacterial infections, and saved thousands of wounded soldiers and civilians in wars and started the era of antibiotics and the subsequent development of new generation antibiotics. The use of systemic antibiotic therapy has been a traditional and common method for eradicating the cause of infection, yet was often unsatisfactory. For example, only a 22–37% effective rate has been reported when combating bacterial infection of medical implants such as catheters and subcutaneous sensors, because most systemic antibiotics did not reach an effective local concentration [2]. However, increasing the administrative doses of antibiotics causes cytotoxicity and side effects in the patient's body. Another serious problem associated with the use of antibiotics is the emergence of multidrug resistance to bacterial strains, which renders current antibiotics ineffective and requires additional interventions such as more radical surgery. Therefore, ways to prevent bacterial infection and mitigate multidrug resistance simultaneously have receiving growing attention.

Nature, however, has evolved ingenious solutions based on topological surfaces to fight bacterial infection in green and efficient manners. Typical examples of natural surfaces that exhibit antibacterial properties include the lotus leaf, wings of cicadae, wings of dragonflies, wings of planthoppers, springtail skin, shark skin, and gecko feet. Unlike antibiotic treatment, natural surfaces can physiochemically minimize bacterial infection by interfering with the surface–bacteria interaction, which fundamentally avoids the evolution of multidrug resistance [1][10][11][12][13][14][15][16][17][18].

2. Natural Bacteria-Repellent Surface

A bacteria-repellent surface is usually achieved by introducing superhydrophobicity to remarkably lower bacterial adhesion. Superhydrophobic or the so-called self-cleaning surfaces can be widely found on plant leaves, insect cuticles, fish skin, etc., which enable these species to passively control bacterial colonization. For example, a lotus leaf was the first reported to have superhydrophobicity and bacterial repellence [19]. The underpinning mechanism was the combination of low surface energy and the multiscale roughness of surface lipid structures, which allowed the surface to have a high water contact angle (θ* 150°) and a low sliding angle (θ_S 10°), and trapped large amounts of air cushion, which significantly minimizes the surface/bacteria contact. Bacterial cells colonizing such surfaces would be removed before they had a chance to form biofilms [20]. Similar phenomena have also been observed on some insect surfaces, such as planthoppers and springtails [21]. Planthoppers' hindwings feature topographical and functional similarities to lotus leaves, thus exhibiting non-wetting behavior and low adhesion to pollutants [22][23]. Springtail skin is another kind of superhydrophobic surface consisting of a microcolumnar with a double nanoreentrant [24][25][26]. The superhydrophobic skin endowed it with an anti-adhesion property to protect springtails from bacterial attaching and infection [27]. Shark's hydrophobic skin, leveraging flat scales or dermal denticle arrays, offers another ingenious strategy to prevent the attachment and growth of microorganisms, with additional benefits in drag reduction [28][29][30][31].

3. Natural Contact-Killing Surface

Unlike the bacteria-repellent strategy, many other biological surfaces violently kill the bacteria in contact with them. The contact killing effect lies in that their extremely fine structures can pierce the cell membrane due to the concentrated mechanical stress and gradually rupture the cell. While varying in shape and other properties, the common feature of these natural contact-killing surfaces is their pattern in nanoscale size (50–250 nm) and two-dimensional arrangement [32]. For example, A cicada wing's surface has uniform nanocone arrays with a height of 200 nm, a top diameter of 60 nm, a bottom diameter of 100 nm, and an interpillar space of 170 nm. Unlike the lotus leaf, a cicada wing is a surface manifesting a large water contact angle of 158.8° but a high degree of bacterial adhesion. Bacteria on such a surface can be pierced through by the nanotopography [33]. Specifically, bacterial cell membranes that contact the surface patterns bear a large stretching force, accompanied by a sharp increase in the total membrane area, which collectively results in irreversible membrane rupture and bacteria death [34][35][36]. Gram-positive cells have thicker layers of peptidoglycan and are therefore generally more rigid, which may explain their increased resistance in comparison to Gram-negative cells. This is why cicadas' wings are only effective against Gram-negative bacteria. Such functional shortcomings can be well tackled by the surface of dragonfly wings, on which both Gram-negative bacteria (*P. aeruginosa*) and Gram-positive bacteria (*S. aureus* and *Bacillus* sp.) and even endospores can be mechanically ruptured. A dragonfly wing is also covered with high aspect-ratio nanostructures that can pierce almost all bacterial membranes in contact with it [37][38]. A gecko with a unique hair structure has drawn much attention due to its superhydrophobicity and associated topographical antimicrobial effects [39]. The gecko's skin is composed of small hairs (often called spines or microspines) a few microns in height, with an interspace of 0.2–0.7 μm. Because gecko hair possesses a tip shape and size similar to the nanocones on cicadas, it can be an alternative for studying antimicrobial properties. Gecko skin has been proved to be antibacterial, with a remarkable killing effect on *Porphyromonas gingivalis*, a clinically significant bacterium [40][41].

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