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Electrochemical Methods for the Detection of Antimicrobial Resistance and Multi-Drug Resistance Bacteria

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Abstract

Accurate diagnosis of bacteria is one of the most important stages of the definitive treatment of bacterial infections. However, due to the Antibiotic Resistance (AR) that has recently emerged in bacteria, not only the diagnosis of bacteria but also the determination of the antibiotic resistance has become extremely important. For the determination of AR of bacteria, classical microbiological and biochemistry methods are already applied. However, these methods have many disadvantages in terms of cost and time. With advances in technology as well as molecular biology, a new era has emerged for the accurate determination of AR in bacteria as well. For example, electrochemical methods have been developed recently for the label-free diagnosis of both bacteria and their AR. In this we focus on the issues regarding AR of bacteria and their diagnostic significance. Herein, we also focused on the electrochemical method used for the diagnosis of bacteria and AR.

Keywords: Bacterial infections; Antibiotic resistant bacteria; Label-free diagnosis method; Electrochemical detection

Description

Microbial infections have been one of the most mysterious diseases throughout history, causing fearful epidemics for human beings, like SARS-CoV-2 of our time. Discovering the origins of these diseases and also combating them have been a mystery to humans for centuries [1]. The fact that these diseases were caused by single cells was clearly determined after the discovery of the microscope. Later, the structural features of these organisms were determined and classified as prokaryotic cells. Although many bacteria have been identified with microbiological diagnostic methods, the definitive detection of these bacteria has required a great effort. With the development in biochemistry and microbiology, more reliable diagnosis of bacteria has become possible, but it has shown limitations in terms of cost and time [2]. It has been traditionally known that some substances are effective against infections. Later, the chemical structures of these substances called antibiotics were determined and have been the focus of pharmaceutical research. Although antibiotics have achieved great success against bacterial infections, unfortunately it has also led to the resistance of bacteria against them due to their irregular and excessive use. Therefore, bacteria detection was no longer sufficient, and the selection of an effective antibiotic treatment has been emerged to huge challenge stage. As a remedy, in addition to the existing methods for bacterial diagnosis, it has become necessary to carry out Antibiotic Susceptible Tests (AST) carefully for each bacterial case [3]. As a simple example, rifampicin, ethambutol, streptomycin and isoniazid antibiotics, which have great efficacy against *Mycobacterium tuberculosis* responsible for tuberculosis disease infection, have recently been shown to be ineffective. Although this resistance is often against only one antibiotic, it is sometimes seen for more than one [4]. This situation is known as Multidrug Resistance (MDR). Treatment strategies against bacteria with MDR characteristics are limited and often present dangerous situations that may result in death. Therefore, an effective antibiotic should be selected urgently.

Although there are conventional tests for AST today [5], early diagnosis is not possible with these methods (especially in bacteria with low growth rates). Today, AST are performed faster and more reliably with molecular methods that have emerged with the development of technology. The logic of these methods is to perform antibiotic testing at the molecular level (at the gene level). Polymerase Chain Reaction (PCR) provides several advantages including fast and sensitive detection. However, this technique lacks satisfying capacity for multiplexing as well as fast tracking (from sample collection to results, can take 5-24 hours and cost more than 45 Pounds) [6] as an alternative approach, the microarray techniques utilize the specific molecular probes in the AST. Despite their broad-spectrum characteristics, the microarray techniques have several limitations including high cost, relatively low accuracy due to non-specific binding caused by DNA probes, and time-consuming procedure [7].

Recently, electrochemical methods for the detection of bacteria and AST have become the focus of research by many groups [8-10]. Diagnosis of bacteria is possible at the whole-cell or gene level through this method in high sensitivity, while the resistance can be studied even at the molecular level [11]. Although there are many techniques for detecting and measuring electrochemical changes, Electrochemical Impedance

Spectroscopy (EIS) is widely used which captures changes in phase and amplitude as signal passes through the system [12].

The working mechanism of this method is based on the electrochemical measurement that occurs during the molecular bonding on the surface. Accurate determination of the resistance can be made as a result of changing the surface chemistry with molecules such as oligonucleotides, proteins etc. belonging specifically to a particular bacterium. For this purpose, the electrode surfaces are modified with specific probes. These probes need to be specifically designed to bind only to the oligonucleotide or protein of a unique bacterium. The potential of label-free determination of analytic through this method is an undisputed advantage that make this technique more appropriate in terms of efficiency, cost, and time. Sensitivity of the technique towards mutant changes is highly sufficient to prove the susceptibility level of the bacteria towards a particular antibiotic. Thanks to these features, it promises for the development of new systems for the diagnosis of bacteria and, most importantly, for performing multiple AST, simultaneously in less than 2 hours of assays time.

Conclusion

Today, determining AR in bacteria plays an extremely important role in order to choose a definitive antibiotic therapy. Although classical methods are widely used for the diagnosis of bacteria and determination of AR, it is a certain fact that they are insufficient in terms of cost, reliability and time. Therefore, with the advances in new technologies, new approaches, like electrochemistry-based label-free methods, will be more advantageous for the determination of antibiotic resistance at the molecular level. Plus, combination of these techniques with other platforms, like microfluidics, would pave the way for quicker on-field tests to be performed easily everywhere, whereas comparative studies with molecular dynamic simulations, crystallography would provide exclusive details on the resistance development.

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