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ELECTROCHEMICAL SENSORS FOR THE DETECTION OF CHEMICAL WARFARE AGENTS: STRATEGY AND EXEMPLES

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Abstract: *Since the addition of chemical warfare agents (CWAs) in the World War I, there has been a constant demand for the development of rapid and accurate analytical instruments for detecting and identifying these agents. The most common techniques used in CWAs determination are spectroscopic and chromatographic techniques. Although they possess remarkable robustness, they require prolonged analysis time, experienced personnel, expensive instrumentation and are not fit for on-field applications and fast early alert. Fortunately, electrochemical sensors represent a viable alternative due to their, simple instrumentation, high sensitivity and low cost. The aim of this article is to highlight some important aspects of electrochemical sensing and to present some electrochemical sensors developed for CWAs detection. The future perspectives and challenges in electrochemical sensor development for CWAs detection is also discussed.*

Keywords: chemical warfare agents, electrochemical sensors, Fast determination, Recognition element, Biosensors

1. Introduction

Chemical warfare agents (CWAs) are very toxic substances used for their capacity to kill, incapacitate, or control enemies. With advancements in science and chemistry, in the last century, more than 70 different chemicals have been developed and produced [1,2].

The first full-scale use of CWAs began in WWI, when the German Army released 16-tons of chlorine gas over the opposing French trenches [3]. During WWI, almost 80000 fatalities and 1.3 million non-fatal casualties were due to the use of chemical warfare agencies [1]. Since then, CWAs have been prohibited, but they are still being used in terrorist attacks and widely stocked [4].

Today, due to their facile synthesis by simple chemical reactions, several terrorist organizations and more than 25 countries possess CWAs, and many other organizations are seeking to obtain them [1]. CWAs can be classified based on their toxicity and biological mechanism of action in: nerve agents, blood agents, blister agents and choking agents [5].

Given their potential threat, it is crucial to develop reliable methods that allows the detection and identification of CWAs. Rapid on-site detection and laboratory analysis after on-site sampling is imperative and can lead to effective measures for military and civilian protection [6].

Many efforts have been made to determine and quantify CWAs in a quick, precise, convenient, and economical fashion. Currently, there are many analytical techniques that have successfully used to detect CWAs. The most popular strategy involves the use of spectroscopic (ion mobility spectroscopy, FT-IR spectroscopy)

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and chromatographic techniques (gas chromatography, liquid chromatography) [7]. However, most of these techniques present several limitations, such as prolonged analysis time, complicated extraction or derivatization and expensive instrumentation. Fortunately, electrochemical sensors represent a feasible alternative due to their simple instrumentation, high sensitivity, fast response and low cost [8,9]. Additionally, they allow miniaturization, real-time detection, and field portability, making them excellent for on-site monitoring of CWAs.

2. Electrochemical sensors

Electrochemical sensors are devices that convert the biochemical reaction into an analytically useful signal. Any electrochemical sensor consists of two basic components: a recognition element that is fixed at the electrode surface and a transducer. The recognition element is the most important component of the sensor and oversees the selective recognition of the target analyte. Then, the transducer transforms the interaction between the analyte and the recognition element into an electric signal that can be detected (Fig. 1).

2.1. Types of electrochemical sensors

Based on the operating system of the transducer, electrochemical sensors are classified in:

- Conductometric, measuring the system ability to carry an electric current.
- Potentiometric, measuring the potential difference between two electrodes (working and reference electrode).
- Voltammetric, measuring the current as a function of applied potential.

According to their recognition element, electrochemical sensors can be classified in:

- Chemosensors, which uses a synthetic molecule for signalling the presence of matter or energy.
- Biosensors, which uses a biological element to detect the analyte [10].

2.2. Recognition elements in electrochemical sensing

Recognition elements are the crucial parts of electrochemical sensors, as they provide the selectivity that allows the sensor to selectively respond to a particular analyte or group of analytes, while avoiding interference from other substances.

The recognition element employed for the development of an electrochemical sensor is chosen depending on the structure of the target analyte in order to achieve higher affinity for the target and appropriate stability.

A wide variety of natural and synthetic recognition elements have been successfully exploited in electrochemical sensing for laboratory and field-based applications.

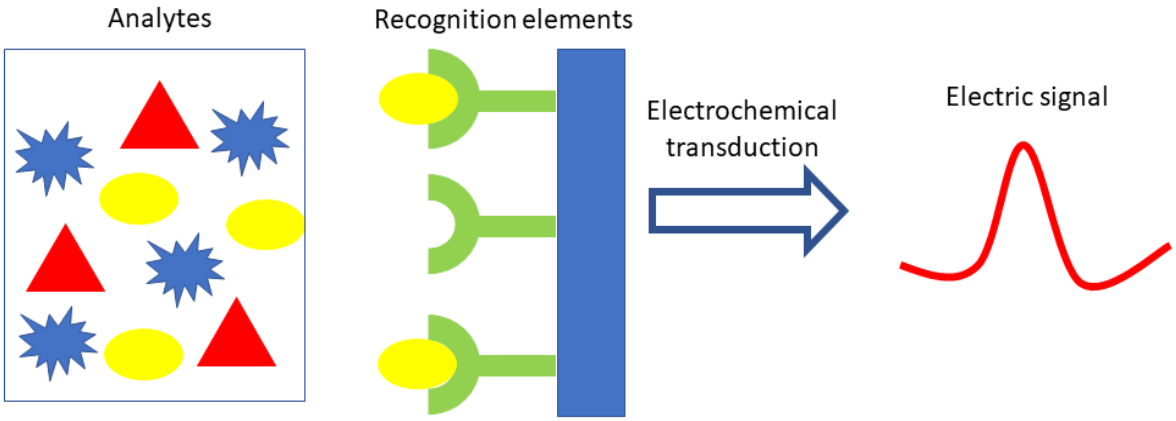


Figure 1: The structure and basic principle of an electrochemical sensor

Biological receptors have extraordinary affinity and specificity, but their use as recognition elements is typically hindered by their poor chemical and thermal durability, as well as their expensive prices. However, in the last decades the availability of biological receptors has significantly improved, and several biologically derived materials have been successfully used in electrochemical sensing, such as nucleic acids, aptamers, antibodies, enzymes, or even whole cells. Nowadays, new synthetic recognition elements have been developed due to their characteristics, such as stability and selectivity, or low cost. More so, their structure can be tailored for a wide range of analytes. For example, different small and medium molecules, metallic nanoparticles, carbon nanomaterials, molecularly imprinted polymers, cyclodextrins, calixarenes and various ligands have been integrated in sensors design [11].

Different techniques have been used to anchor the recognition elements at the electrode surface, such as: drop – coating, covalent binding, self-assembly, electropolymerization, electrodeposition and sol-gel encapsulation. Among them, the most common are drop-coating and electrodeposition [12].

2.3. Development of electrochemical sensors

Several essential criteria must be assessed when deciding if electrochemical can be utilised and, if so, what type of sensor and technique is best (Fig. 2). This will enable to determine if electrochemical sensors are a good and viable substitute to other techniques, taking into account not only the targeted analyte but also the matrix in which exists [13,14]. Therefore, a useful electrochemical sensor must meet a set of experimental design criteria to reach its potential benefits. Among the most crucial are:

- Each electroactive species undergoes a redox reaction at a specific potential. Applying a specific potential in voltametric or amperometric sensing can lead to high selectivity and specificity.
- Low detection limit and High signal-to noise ratio.
- The measurements are accurate, reliable, and repeatable.
- Calibration is not needed or is easy and simple to perform.
- Fast response time and the decrease of sensor response with time is small.

The impact of these factors depends on electrode and type of transducer used, cell configuration and monitoring necessities.

However, it is also important to consider the opportunities and advantages that arise from:

- Miniaturization and incorporation in flow systems for online monitoring.
- Portability which allows the sensors to be used outside the laboratory.
- No pre-treatment or sample digestion is needed [13,14].

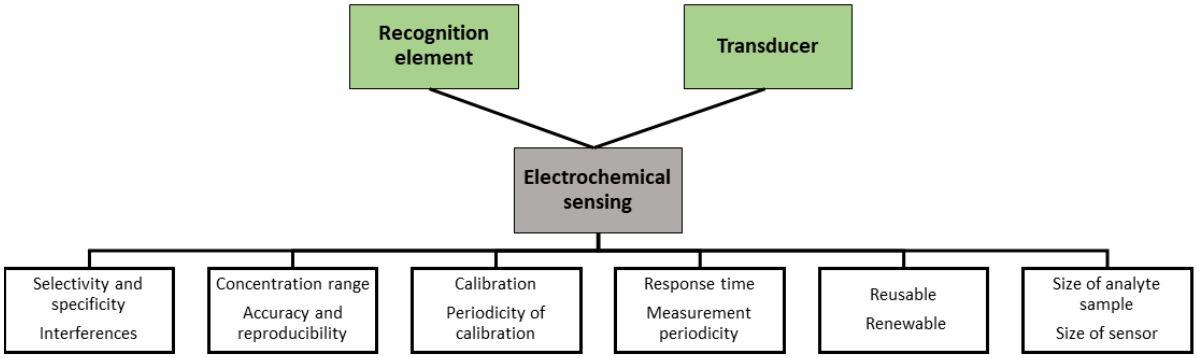


Figure 2: Important aspects for choosing electrochemical sensing [13,14]

3. Electrochemical sensing of CWAs

The customization of electrochemical sensors with suitable recognition elements and transducers has created an opportunity to develop diverse types of sensors for various applications, belonging to numerous areas, including the medical, pharmaceutical, environmental, and defence ones [15]. The defence sector requires instruments that can identify CWAs fast, using simple procedures, so that suitable countermeasures may be taken in a timely manner. Next, a brief description of CWAs and some electrochemical sensors developed for their detection are reviewed.

3.1. Nerve agents

Nerve agents are a class of CWAs that irreversibly inhibit a key enzyme of nervous transmission (Cholinesterase), therefore causing excess stimulation. All nerve agents are organophosphorus compounds. The most important ones are tabun, sarin, soman and Vx.

Until now, four different types of electrochemical sensors have been developed for their detection based on:

- Cholinesterase enzyme inhibition
- Organophosphate hydrolase enzyme
- Antibody use
- Direct electrochemical detection

The first two types of sensors use enzymes to quantify nerve agents by determining the enzymatic activity in their presence or absence. Several sensors have been developed based on cholinesterase inhibitions, the first been produced in 1962 [16]. Since then, especially in the last decade, various electrochemical sensors have been utilized for nerve agent detection, using various transducers and recognition elements with improved features [17–19].

By replacing cholinesterase with an organophosphate hydrolase enzyme as recognition elements, a faster detection can be obtained but with a lower sensitivity. Until now, various electrochemical sensors have been developed based on the use of organophosphorus hydrolase as receptors, with the detection limit of approximately 0.1 μM [20–22]. However, the commercial application of enzyme-based sensors has been obstructed by the high cost of enzyme extraction, purification, and processing [23].

Antibody-based sensors, known as immunosensors, exploited the specificity provided by antigen-antibody interaction. The use of immunosensors for nerve agents detection has been demonstrated in several studies [6,24,25], offering a new approach for sensitive, selective and rapid determination.

3.2. Blood agents

Blood agents deprive the blood and organs of oxygen. Thus, they cause the body to suffocate. They include arsine, hydrogen cyanide or cyanogen chloride.

Several studies showed that electrochemical detection of blood agents can be realized from a several environmental [26], food products [27], or physiological samples [28].

3.3. Blister agents

Blister or vesicant/blistering agents, are chemical compounds that cause severe irritated skin, resulting in blister, swelling and inflammation. In addition to their acute effects, they can stay in the environment for years after their use. Blister agents include sulfur mustards, nitrogen mustards or lewisite.

Few studies have been focused on developing electrochemical sensors for a fast and easy detection of blister agents [6,29–31]. The results have been promising, showing that electrochemical sensors can be integrated into portable monitoring devices, drones, or military uniforms [31].

3.4. Choking agents

Choking or pulmonary agents are chemicals that are designed to produce serious irritation of the respiratory tract and inducing swelling in those areas. Examples of choking agents include ammonia, bromine, chlorine, hydrogen chloride, phosphine, phosphorus, phosgene, diphosgene, or methyl isocyanate. Phosgene is the most used, being responsible for 80 % of all chemical fatalities during WW I. Also, it is an industrial intermediate in organic synthesis. Thus, there is a continuous need for developing simple and sensitive methods

for phosgene detection for safety against chemical attacks but also for industrial production [6].

Developments in electrochemical methods for phosgene detections are unexpectedly rare, with only one effective sensor being reported in literature [32]. However, this system allowed the detection of phosgene well below the permissible exposure limit.

4. Future perspectives and conclusions

Over the past few years, the development of electrochemical sensors for CWAs detection has gained the interest of many scientists as an alternative to the conventional methods of detection. Electrochemical sensors can be a feasible alternative for the detection of CWAs due to their unique properties, such as high sensitivity, fast response, low cost, and simple instrumentation. More so, they are compatible with miniaturization and portability.

However, despite the considerable progress made in the development of electrochemical sensors capable of detecting CWAs, several challenges still need to be overcome before these systems can be successfully used in real world applications. Sensor's development still must overcome some technical problems, such as the interaction with matrix components, low reproducible fabrication of numerous sensors, short, limited shelf life. More so, the translation of electrochemical sensors from academic to clinical applications faces numerous obstacles and they still need to exhibit applicability in real samples and in feasible scenarios where the selectivity, stability and robustness of the sensor can be challenged.

Nevertheless, it is necessary to remember that electrochemical sensing is still somehow new, and many shortcomings will be solved with the cooperation of researchers from several areas of knowledge, greater financial investment, or advances in nanoscience and nanotechnology. Current development show that electrochemical sensing may be a viable option for field applications and fast early warning in case of CWAs use.

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