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Biosensors based on electrochemical lactate detection: A comprehensive review

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ABSTRACT

Lactate detection plays a significant role in healthcare, food industries and is specially necessitated in conditions like hemorrhage, respiratory failure, hepatic disease, sepsis and tissue hypoxia. Conventional methods for lactate determination are not accurate and fast so this accelerated the need of sensitive biosensors for high-throughput screening of lactate in different samples. This review focuses on applications and developments of various electrochemical biosensors based on lactate detection as lactate being essential metabolite in anaerobic metabolic pathway. A comparative study to summarize the L-lactate biosensors on the basis of different analytical properties in terms of fabrication, sensitivity, detection limit, linearity, response time and storage stability has been done. It also addresses the merits and demerits of current enzyme based lactate biosensors. Lactate biosensors are of two main types – lactate oxidase (LOD) and lactate dehydrogenase (LDH) based. Different supports tried for manufacturing lactate biosensors include membranes, polymeric matrices-conducting or non-conducting, transparent gel matrix, hydrogel supports, screen printed electrodes and nanoparticles. All the examples in these support categories have been aptly discussed. Finally this review encompasses the conclusion and future emerging prospects of lactate sensors.

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1. Introduction

Lactate concentration has been widely used as a key parameter in the clinical diagnostics for assessing patient health conditions and study of diseases and for continuous surveillance in surgery [1,2], sports medicine [3], shock/trauma [4] and food industry [5,6]. The baseline lactate level in blood ranges from 0.5 to 1.5 mmol/l at rest [1] but can rise up to 25 mmol/L during the intense exertion [7]. Lactate is a key metabolite of the anaerobic metabolic pathway. When the energy demand by tissues cannot be met by aerobic respiration, an increase in lactate concentration will occur from the anaerobic metabolism. Without adequate clearance by liver and kidney, the accumulated concentration of lactic acid results in lactic acidosis [8]. So the production and utilization of lactate are tightly controlled by lactate homeostasis in a healthy person. The lactate balance is significant to acid–base homeostasis, as formation of lactate is associated with enhancement in proton concentration inside the cells and the utilization of lactate and regeneration of bicarbonate are required to counter balance the production of proton and the loss of bicarbonate [9]. Such finely tuned interplay of parameters that influences the delicate lactate balancing system is necessary because our body is viable only within an extremely narrow range of pH (between pH 7.2 and 7.4) [10]. Clinically, causes of lactic acidosis can be classified by two ways: type A disorders, in which there is decreased tissue oxygenation such as with shock, left ventricular failure, sepsis and poisoning with carbon monoxide and cyanide; or type B disorders, caused by certain drugs/toxins, along with systemic disease, including failure of renal and hepatic system, diabetes and malignancy or inborn error metabolism [11]. According to Medicare data and published literature in the year 2000, an estimated 4.4 million patients were admitted to ICU in US annually, in which about 25% of the above patients suffered from sepsis (this is due to procoagulant and systemic inflammatory response) [12]. When this condition is combined with one or more vital organ dysfunctions, the patient will develop severe sepsis. The mortality rate of sepsis is estimated around 30–50%, which corresponds to at least 225,000 deaths annually [13,14]. Recent studies have shown that early lactate clearance could improve the treatment outcome in severe sepsis and septic shock, which could potentially lead to the decrease in sepsis related mortalities [15]. Therefore, a patient's blood lactate level may act as alarm signal for the severity of illness and may also be used to improve the diagnosis and treatments of a broad range of diseases. Lactate also has a significant importance in sports medicine, especially for determining physical fitness in athletics. Level of lactate in blood during exercise is used as an indicator for the athletic training status and fitness since elevated levels of blood lactate results in decrease level of pH in blood finally resulting in fatigue.

The importance of lactate estimation also can be found in many food and fermentative industry. Fermentative products such as fermented milk products, wine, cured meat and fish and also pickled vegetables produce lactate. Due to this fact, lactate is commonly used as a specific indicator of the presence of bacterial fermentation, thus as an indicator for the freshness and quality of the food [16].

As mentioned above, it is clear that lactate is a metabolite that has evoked a great interest in many industries for importance of detecting and measuring its existence in various media. Analytical methods, which are most commonly employed for lactate determination, are high performance liquid chromatography (HPLC) [17] with other methods being fluorometry [18], colorimetric test [19,20], chemiluminescence [21] and magnetic resonance spectroscopy [22,23]. Although these methods provide results, these suffer from drawbacks like time consuming requirement of sample pre-treatment, costly due to requirement of expensive machinery and trained manpower. However, biosensors can overcome these limitations. When compared with various methods available for L-lactate detection, biosensing methods possess the advantages of being simple, direct, and real-time with no need of sample preparation (except perhaps for dilution of the sample), combining rapid response with high specificity, economical and are user-friendly [24].

In this present review, we briefly introduced the development and applications of L-lactate biosensors. We also summarized the L-lactate based biosensors by comparing their different analytical properties in terms of fabrication, sensitivity, detection limit, linearity, response time and storage stability. Along with this the merits and demerits of current enzyme based lactate biosensors have been highlighted. Finally this review encompasses the conclusion and future emerging prospects of lactate sensors.

2. Enzymes involved in lactate biosensors

The concept of an enzyme coupled biosensing electrode involves placement of an enzyme in close proximity to an electrode surface. The enzyme involved must catalyse the reaction which involves consuming of electroactive reactant or generation of electroactive species. The depletion or production process is then