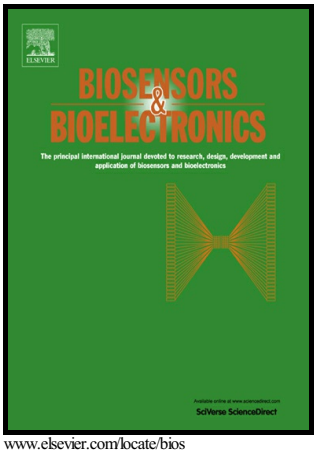

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In-vitro model for assessing glucose diffusion through skin

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Abstract

Pig ear skin membrane-covered glucose biosensor based on oxygen electrode has been assessed as a tool to evaluate glucose penetration through skin *in-vitro*. For this, glucose oxidase (GOx) was immobilised on oxygen electrode and covered with the skin membrane. Exposing this electrode to the solution of glucose resulted in glucose penetration though skin membrane, its oxidation catalysed by GOx, consumption of O_2 and decrease of the current of the oxygen electrode. By processing the biosensor responses to glucose, we found that glucose penetration through 250 µm thick skin membrane is slow; 90% of steady-state current response was reached in 32(±22) min. Apparent diffusion coefficient for glucose in skin was found to be equal to 0.15(±0.07)*10^{-6} cm^2s^{-1}. This value is 45 times lower than glucose diffusion coefficient in water. Tape-stripping of stratum corneum (SC) allows considerably faster glucose penetration. The electrodes covered with tape-stripped skin reached 90% of steady-state current response in 5.0(±2.7) min. The theoretical estimate of glucose flux through SC was considered exploiting four-pathway theory of transdermal penetration. Theoretical flux values were more that three orders lower than measured experimentally. This high discrepancy might indicate that glucose penetration through healthy human skin could be even slower, allowing much lower flux, than it was found in our study for skin membranes from pig ears.

Keywords: glucose biosensor; attachable; skin; topical; epidermal

1. Introduction

The number of people affected by diabetes is constantly growing. Among adults, it has increased from 4.7% in 1980 to 8.5% in 2014 (WHO). Frequent monitoring of blood glucose, followed by an adequate changed life style or/and appropriate use of medication, are the most vital measures that supports management of diabetes (Rise et al. 2013). This is a reason behind the global growth of the glucose biosensor market, which according to Grand View Research Inc. estimate will reach USD 31 billion by year 2022. The majority of blood glucose measurements are done by sampling of blood from a punctured finger, which is regarded as non-convenient and painful (Heinemann 2008; Yoo and Lee 2010). This stimulates tremendous research efforts to develop non-invasive or minimally invasive glucose monitoring approaches as well as implantable glucose biosensors (Kim et al. 2018; Lee et al. 2017; Lheureux and Preiser 2014; Pickup et al. 2011). Development of new medical devices usually rely on high number of clinical trials, which could be minimised if an appropriate *in-vitro* system could be introduced. In this work, we propose and examine a simple tool to study glucose diffusion through skin *in-vitro*. The system consists of an electrochemical glucose biosensor based on an oxygen electrode covered with skin membrane from pig ear. Other biosensor designs relying on