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Smart bandage with wireless connectivity for uric acid biosensing as an indicator of wound status

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ABSTRACT

Advanced wound care technologies need to evolve in response to the growing burden of chronic wounds on national healthcare budgets and the debilitating impact chronic wounds have on patient quality of life. We describe here a new type of smart bandage for determination of uric acid (UA) status, a key wound biomarker, formed by screen printing an amperometric biosensor directly on a wound dressing. Immobilized uricase, paired with a printed catalytic Prussian blue transducer, facilitates chronoamperometric detection of uric acid at a low working potential. The smart bandage biosensor interfaces with a custom designed wearable potentiostat that provides on-demand wireless data transfer of UA status to a computer, tablet, or Smartphone by radio frequency identification (RFID) or near-field communication (NFC). The analytical performance of the smart bandage—sensitivity, selectivity, operational stability, and mechanical robustness—is described. Application of these bandages will provide insight into wound status and may reduce the frequency at which dressings are changed, allowing for healthcare cost savings and a reduction in patient stress and pain.

1. Introduction

Around 2% of people in the developed world will suffer a chronic wound during their lifetime [1]. This alarming figure is rising because of ageing population demographics [2], and chronic venous leg ulcers alone affect 15% of all people aged over 70 years worldwide [3,4]. The United States currently spends $25bn a year on chronic wound care [5] and similarly large sums are spent in most major economies [2, 6–8]. It is clear that wound management represents a significant social and financial burden. Outpatient services are heavily loaded by the costs and resources required for treating chronic wounds. Cost reduction strategies often seek to reduce the number and frequency of dressing changes [9,10]. Moreover, dressing changes cause stress and pain for patients [11]. The argument for advanced wound care technologies to evolve to address these challenges is compelling. Specifically, there is a need for smart bandages that monitor status parameters and that communicate wound status in a clinically relevant and cost effective manner [8]. In doing so, smart bandages will help shift the paradigm of chronic wound care from routine management and time-based dressing changes toward personalized care and knowledge-based treatment.

Sensor research in wound monitoring focuses primarily on generic physiological status indicators: temperature [12,13], moisture [14,15], pH [16–18], pO_2 [19,20], and bacterial load [21,22]. However, uric acid (UA) concentration in wound exudate is highly correlated with wound severity [23,24] and significantly decreases during bacterial infection because of catabolysis by microbial uricase [25]. This makes UA a highly specific indicator of wound status and infection and is why we selected it as a key biomarker for our research.

Bandage-based electrochemical detection of UA has been described elsewhere [25,26]. This non-enzymatic sensor employed square wave voltammetry on a carbon fiber mesh working electrode to detect changes in urate levels. The sensor required a large positive potential on the working electrode to catalyze the oxidation of UA, which could result in interference from other easily oxidized species present in wound exudate. Also, while the potentiostat was portable, it was neither mobile nor wearable. It is apparent that effective data communication by wireless or non-contact means is a prerequisite for the successful adoption and ease-of-use of smart bandages.

We describe the development and analytical characterization of a novel amperometric bandage-based UA biosensing system with non-contact wireless connectivity, Fig. 1. The new wearable UA biosensor has been fabricated by screen-printing Prussian blue (PB) modified

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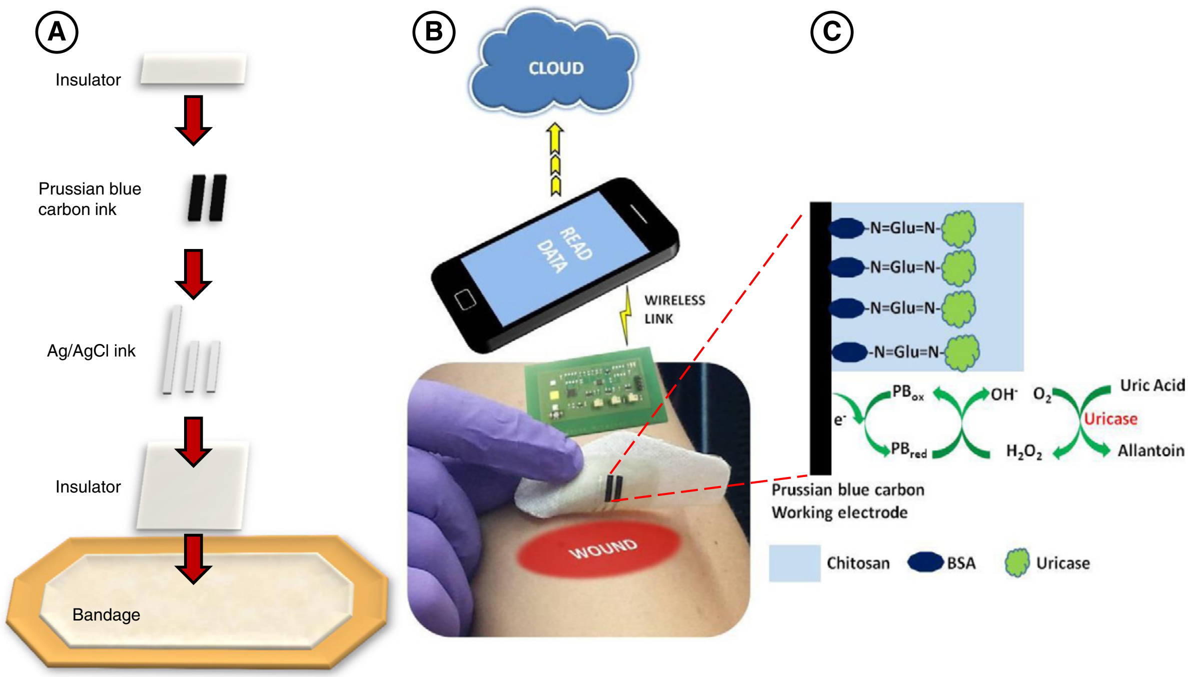

Fig. 1. (A) Screen printing the smart bandage. (B) Wearable potentiostat determines UA concentration and wirelessly communicates with a computer or Smartphone. (C) Schematic showing amperometric detection of UA with uricase immobilized on PB working electrode.

carbon electrodes onto a commercial bandage, and immobilizing the enzyme urate oxidase (uricase) on the working electrode. The enzyme provides highly specific oxidation of uric acid and the PB-carbon electrode catalytically reduces the hydrogen peroxide product of UA oxidation. This enables sensitive and specific detection of UA at a very low negative working potential. The bandage connects to a novel potentiostat developed specifically for use with mobile and wearable biosensors and which has integral wireless capability. The potentiostat autonomously measures and stores the biosensor current output which is proportional to UA concentration. Upon request, data are wirelessly transferred from the potentiostat by radio frequency identification (RFID) to a computer, or by near-field communication (NFC) to a Smartphone or tablet.

2. Materials and methods

2.1. Reagents and instrumentation

All chemicals were from Sigma-Aldrich (St. Louis, MO). Uricase was from *Candida*, bovine serum albumin (BSA), glutaraldehyde solution (8%), and chitosan were used in the sensor fabrication. Uric acid, creatinine, D-(+)-glucose, L-(+)-lactic acid, L-ascorbic acid, and 0.1 M phosphate-buffered saline, pH7 (PBS), prepared from K_2HPO_4 and KH_2PO_4, were used in characterization experiments. Electrochemical characterization was performed with CH Instruments (Austin, TX) 440 electrochemical analyzer and the wearable potentiostat. The wearable potentiostat is credit card sized and powered from a button cell. It contains an RFID/NFC interface for wireless data transfer to a computer, Smartphone, or tablet. The electronics is described elsewhere [27].

2.2. Smart bandage biosensor fabrication

Smart bandage biosensors were fabricated by screen printing, Fig. 1A. First, a transparent insulator layer was printed on the bandages and cured at 120 °C for 20 min. The subsequent printing steps, in which an Ag/AgCl pseudo-reference electrode and PB-carbon working and counter electrodes were fabricated, are described elsewhere [28]. Finally, another insulator layer was printed and cured to coat the conductive tracks and to define the working electrode area. The working electrode was functionalized by drop casting 3 μL of a solution consisting of 1 wt% BSA, 0.5 wt% glutaraldehyde, and 15 mg/mL uricase in PBS. After drying at room temperature, the electrode surface was drop coated with 3 μL of 0.5 wt% chitosan solution.

2.3. Sensor characterization experiments

In vitro experiments were performed by dispensing 200 μL of phosphate-buffered saline onto the sensing area of the bandage. Smart bandages were connected to the electrochemical analyzer or wearable potentiostat with microclip connectors. Chronoamperometric measurements were made at −0.3 V vs. Ag/AgCl. The working potential was selected based on cyclic voltammetry of the PB-carbon transducer. During experimental work, the wearable potentiostat collected data at a sample rate of 0.80 s^{-1}. Redox current values were digitized and stored to internal memory, and on completion of the experiment transmitted to a computer fitted with a desktop RFID reader. Chronoamperograms were plotted on the computer in MS-Excel (Microsoft Corp, Redmond, WA). The final steady-state current was taken as the average of 10 data points recorded around $t = 60$s.

3. Results and discussion

3.1. Smart bandage design

The new UA biosensor was fabricated by screen printing directly onto the soft fabric of a bandage, followed by functionalization of the working electrode. The scheme in Fig. 1C illustrates immobilisation of uricase on the working electrode through glutaraldehyde cross-linking with BSA, and the operating principle of the biosensor. Hydrogen peroxide, generated by the enzyme catalyzed oxidation of UA, is selectively reduced by PB, and the reduction current, which correlates to UA concentration, is recorded by the potentiostat. The biocompatible chitosan layer was applied to reduce leaching of the sensor constituents into the sample medium. The analytical performance of the smart bandage