POINT-OF-CARE LITHIUM MONITORING IN WHOLE BLOOD USING A DISPOSABLE, PREFILLED AND READY-TO-USE CAPILLARY ELECTROPHORESIS MICROCHIP

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ABSTRACT

This paper describes a microfluidic capillary electrophoresis device with integrated conductivity detection. The device satisfies all major requirements for point-of-care testing, i.e., simple handling, low sample volume, fast measurements, clear readout, and inexpensive disposable cartridge usage. The system is currently being utilized and commercialized for monitoring lithium in whole blood, however, can potentially be applied to various other ions present in blood, urine or other bodily fluids. The chip contains a single inlet only and will be shipped prefilled with background electrolyte, sealed and blistered; ready for use at the patient's place. A single droplet of blood is required to be placed inside the cartridge to perform the analysis typically within a couple of minutes.

KEYWORDS: Capillary electrophoresis, Point-of-care, Lithium

INTRODUCTION

Usually, the handling and filling procedures of microfluidic capillary electrophoresis (μCE) chips involve extensive pretreatment and fluid pipetting steps. Open reservoirs are connected to the channels enabling flushing, filling and simple electrical connection. Such devices were used to demonstrate proof-of-principle for the separation of various compounds [1]. However, the extensive handling and preparation procedures, non-portable power supplies and detection hardware, make these systems not applicable for point-of care testing. Alternatively, μCE chips were reported with integrated pumps and multiple channel configurations, eliminating the need for manual handling procedures and aiming for a fully automated process [2]. However, as a side effect more controlling and hardware is required.

In this extended abstract a new approach is presented. A glass μCE chip is used containing only a single injection inlet and integrated high voltage as well as conductivity detection electrodes in closed reservoirs (figure 2). To our knowledge this is the first time a single-inlet and prefilled μCE system is applied and whole blood measurements reported. A single inlet device puts higher demands on fabrication, prepackaging, shelf life and shipping. However, it allows for very simple and fast operation ideal for point-of-care testing. This device is used for monitoring the lithium level in whole blood [3]. Lithium, which is not naturally found in the human body in significant amounts, is widely used in the treatment of manic-depressive mood disorder. However, the therapeutic window is very narrow and therefore pre-

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cise monitoring very important. The shown device allows for point-of-care blood analysis at the patient's place. The measurement is usually performed within a couple of minutes.

RESULTS AND DISCUSSION

As can be seen in figure 1 and figure 2, the device is a cartridge based system with the microfluidic glass chip embedded into a polypropylene housing for ease of handling. A blood droplet is acquired by a simple finger prick and placed inside the cartridge. This is then placed into the MedimateMultireader. By electrokinetic transport ions present in the blood droplet are injected into the prefilled glass chip and subsequently separated by capillary zone electrophoresis. The integrated platinum electrodes inside the separation channel connected to a conductivity detector measure impedance changes as separated ion zones pass by. The peak surface, amongst other parameters such as temperature and sampling time, is proportional to the amount of lithium present in the blood. The Medimate Multireader full fills well the required specifications for lithium detection as shown in figure 3, in which measurements were compared with the traditional flame photometer method.

A closed and prefilled microfluidic system, as presented here, puts new demands on design aspects to fullfill shipping requirements and shelve life. In order to compensate for thermal fluid expansion a gas bubble (app. 0.5µL in volume) was integrated. As shown in figure 2 in the close-ups, the integrated gas bubble shrinks as the encapsulated fluid expands with an increasing environment temperature (here: 22°C to 70°C).

Figure 1. Lithium measurement: a) shipped blister including the prefilled µCE chip assembled into a plastic disposable for ease of handling and sample application b) application of a single blood droplet c) disposable inserted into the Multireader including high voltage power supply and conductivity detection unit. The measurement is done typically within 2 minutes.

Furthermore, to prevent gas bubble formation caused by electrolysis at the electrodes inside the closed reservoirs, the fluid volume in the electrode reservoir has been precisely matched so that generated hydrogen and oxygen stays soluble within the measurement time.

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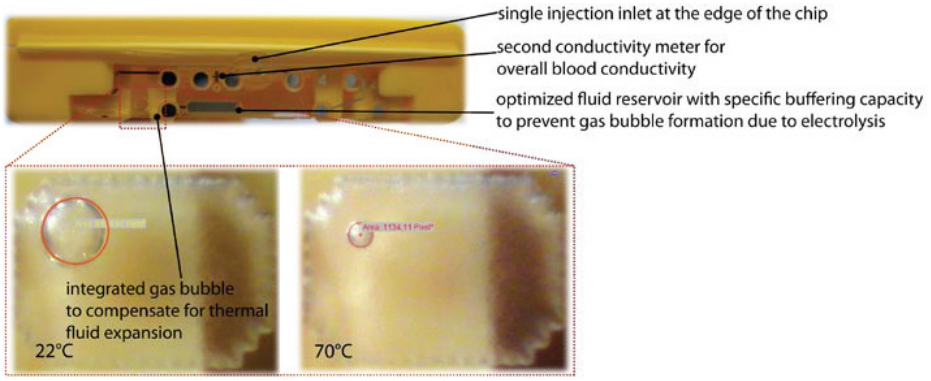

Figure 2. Microfluidic glass chip for capillary electrophoresis with integrated conductivity detection. The chip is 4mm high and 28mm long. It contains a single injection inlet and closed electrode reservoirs and is prefilled with fluid, allowing fast and simple measurements. Chip layout (red: microfluidic channels, green: Pt electrodes, blue cavities and openings) including some details, e.g., integrated gas bubble to compensate for thermal fluid expansion, secondary conductivity detection for blood sample, specifically designed fluid reservoirs to prevent gas formation due to electrolysis.

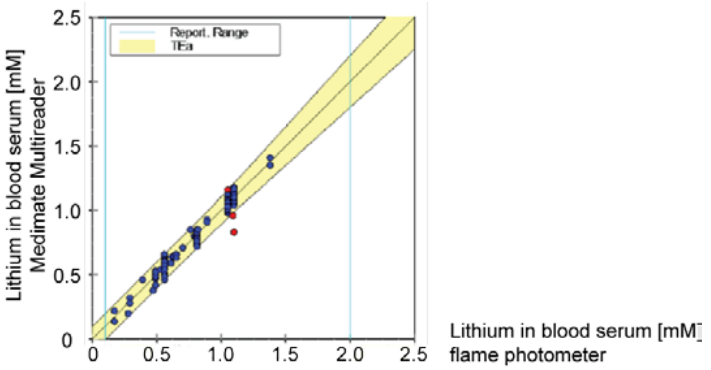

Figure 3. Comparison chart for lithium determination in blood serum between the Medimate system based on microfuidics and the conventional flame photometer method.

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