Sensors and Actuators B 181 (2013) 187–193

Contents lists available at SciVerse ScienceDirect

Sensors and Actuators B: Chemical

journal homepage: www.elsevier.com/locate/snb

Development of photopolymerized fluorescence sensor for glucose analysis

Soner Çubuk[a,*], Ece Kök Yetimoğlu[a], M. Vezir Kahraman[a,*], Pınar Demirbilek[a], Melike Fırlak[b]

[a] Faculty of Art and Science, Chemistry Department, Marmara University, İstanbul, Turkey
[b] School of Pharmacy, İstanbul Kemerburgaz University, İstanbul, Turkey

ARTICLE INFO

Article history:
Received 16 October 2012
Received in revised form 28 January 2013
Accepted 2 February 2013
Available online 14 February 2013

Keywords:
Glucose analysis
Optical sensor
Fluorescence
Membrane
UV-curing

ABSTRACT

The sensing membrane was prepared by photopolymerization of 4-vinylphenylboronicacid (VPBA), hydroxyethylmethacrylate (HEMA) and poly(ethylene glycol) diacrylate (PEG-DA). The membran is capable of determining glucose between 2.78×10^{-4} mM and 5.56×10^{-3} mM with a limit of detection of 0.89×10^{-5} mM, and limit of quantification 3.17×10^{-3} mM ($n = 7$). It can be completely regenerated by using distilled water. The sensor performance characteristics such as response time, dynamic working range and sensitivity were reported. The proposed sensor was then applied successfully for the determination of glucose in blood samples.The optical sensor was stable, cost effective, easy to prepare, rapid and simple for the determination of glucose.

1. Introduction

There is a strong demand for developing a new method for the estimation of total carbohydrate concentration, especially in the diabetic field. Between carbohydrates, glucose plays a main role in various metabolic processes. Especially, the monitoring of glucose concentration in blood or urine for diabetes mellitus patients and also the monitoring of cell growth in biotechnology and fermentation processes call for novel selective and sensitive method. Several analytical techniques are currently used for determination of carbohydrates such as chromatographic techniques [1–5], near infrared spectroscopy [6], spectroscopy [7], amperometry [8,9], optical rotation, electrophoresis, colorimetry and electrochemistry [10]. In addition to these techniques, sensors are most attractive techniques with their sufficient selectivity to target carbohydrate molecules in any food matrix [11]. Sensors are also divided into several types such as, enzyme or enzyme-free sensors [12], electrochemical sensors [13], spectrophotometric sensors [14,15], colorimetric sensors [16,17], diffraction resonance sensors and fluorescent sensor [13,18,19]. Among these types of sensors, fluorescent sensors have had a large success in the past 20 years with their commercial availability and applicability to detect several species. On the other hand, fluorescence measurements have some advantages. Advantages of fluorescence measurements can be listed as (1) extremely sensitive; (2) do not cause any damage to the host system; and (3) measurements also can be made of fluorescence decay times. In addition to these advantages polymer films are frequently used in biosensors to increase permselectivity and also polymer films may be tailored over wide a range of characteristics because of their chemical and physical properties. Polymer films can be tailored with several chelators which are selective to target molecules. Among the chelators the boronic acid moieties are known over 100 years and can be used as a recognition element used for the determination of glucose [20]. There have been several boronic acid based glucose sensing membranes reported in the literature [21–26]. Boronic acid and its derivatives have advantages in glucose sensing: (1) can be tailored; (2) can bind with glucose reversibly, therefore, regeneration of sensor is easily achieved; and (3) relatively inexpensive [10,24]. In this respect, boronic acid based fluorescence membranes are promising for detection of glucose.

This article concerns a new boronic acid based fluorescence sensor for the determination of glucose. Herein, we have synthesized, characterized a novel glucose sensing membrane and we also discussed the membrane's applications to synthetic and real samples. The glucose sensing membrane shows good stability and sensitive response for analytical applications. The sensor developed has been successfully employed for the determination of glucose in real human serum samples and compared with the results of clinic it was shown that glucose could be measured with high accuracy in blood samples.

* Corresponding authors. Tel.: +90 216 3487759; fax: +90 216 3478783.
E-mail addresses: sonercubuk@marmara.edu.tr (S. Çubuk), mvezir@marmara.edu.tr (M.V. Kahraman).

0925-4005/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.snb.2013.02.004

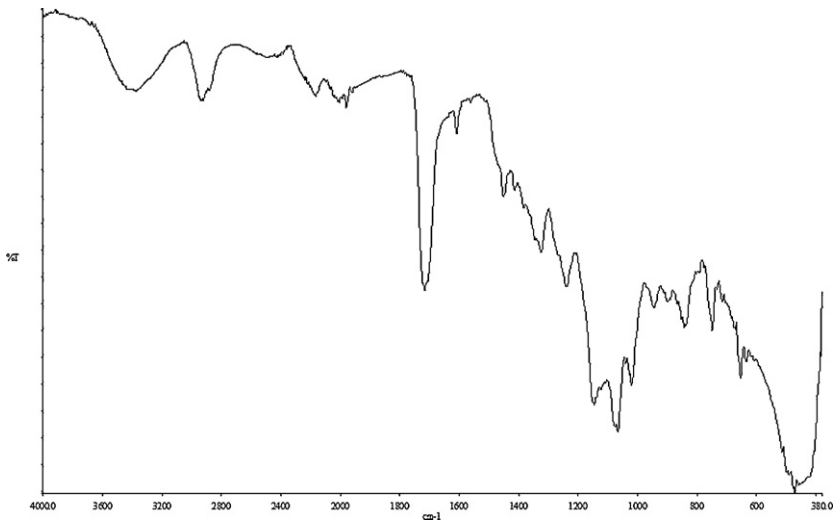

Fig. 1. FTIR spectrum of P(VBPA/HEMA/PEG-DA) membrane.

2. Experimental

2.1. Materials and reagents

The commercial monomers hydroxyethylmethacrylate (HEMA), the crosslinker poly(ethylene glycol) diacrylate (PEG-DA), and the photoinitiator, 2,2-dimethoxy-2-phenylacetophenone (DMPA) and 4-vinylphenylboronic acid (VPBA), were purchased from Sigma. The four sugars, glucose, fructose, galactose and maltose, were purchased from Merck. All the other chemicals such as acetaminophen, uric acid, ascorbic acid and buffer components were of analytical grade and used without further purification. The pH values of the solutions were checked using a digital pH meter (WTW) calibrated with standard buffer solutions of Merck. All of the experiments were operated at room temperature, $25 \pm 1\,^{\circ}C$. All water used in the experiments was purified using a Milli Q-water purification system (Millipore, İncekaralar-Turkey). The resulting purified water has a specific conductivity of 18.2 MΩ cm.

2.2. Preparation of boronic acid based fluorescence sensor

The polymer film based on 4-vinylphenylboronic acid (VPBA) and hydroxyethylmethacrylate (HEMA) were synthesized by free radical crosslinking copolymerization with a small amount of poly(ethylene glycol) diacrylate (PEG-DA) as a crosslinker and 2,2-dimethoxy-2-phenylacetophenone (DMPA) was added as a photoinitiator. The membranes were prepared by UV-curing technique as follows. Polymeric membrane containing 10% VPBA, 70% HEMA, 20% PEG-DA and 3% DMPA. Before UV-curing process, the formulation was purged with nitrogen gas for 15 min to eliminate dissolved oxygen in the system. Then, homogenous mixture was poured into as rectangle teflon molds ($W \times L \times D$: 12 mm × 40 mm × 2 mm). Finally, the formulations were irradiated 300 s under high pressure UV lamp (OSRAM 300 W, λ_{max} = 365 nm).The UV-cured membranes were taken out from the mold and immersed in a large excess of deionized water for 1 day to wash out any unreacted monomers and initiators and then dried in a vacuum oven at 30 °C until reaching a constant weight.

2.3. Characterization

The functional groups of synthesized membrane were analyzed by Attenuated Total Reflection Infrared Spectroscopy (Perkin-Elmer ATR-FTIR spectrophotometer) in the range of 4000–400 cm^{-1}. SEM imaging of the hydrogel was performed on a Philips XL30 ESEM-FEG/EDAX. The membranes were initially dried in vacuum air at 30 °C for 3 days before being analyzed. The specimens were prepared for SEM by freeze fracturing in liquid nitrogen and applying a gold coating of approximately 300 Å. The surface of the sample was then scanned at the desired magnification to study the morphology of the membranes.

3. Results and discussion

3.1. Characterization of the prepared membrane

3.1.1. FTIR spectroscopic studies

In order to identify the polymeric structure, FTIR spectrum of P(VPBA/HEMA/PEG-DA) membrane was taken (Fig. 1). As it can be seen from FTIR spectra of P(VPBA/HEMA/PEG-DA) membrane has the characteristic absorption peaks at 3396 cm^{-1}, 2924 cm^{-1}, 1717 cm^{-1}, 1607 cm^{-1}, 1414 cm^{-1}, 1322 cm^{-1}, 1067 cm^{-1}, 1019 cm^{-1}, and 896 cm^{-1} respectively. These typical characteristic peaks indicate that VPBA and HEMA groups were attached to the membrane structure [20]. These can be summarized as the peak at 3396 cm^{-1} shows the hydroxyl group of HEMA and VPBA, the peak at 2924 cm^{-1}which is due to the presence of —C—H band, the strong peak at 1717 cm^{-1} indicates the carbonyl group of HEMA, the peak at 1607 cm^{-1} shows C=C stretch of aromatic ring, the peak at 1414 cm^{-1} corresponding to aromatic rings with boron attached directly, the peak at 1322 cm^{-1} indicates the B—O stretch, the peak at 1067 cm^{-1}shows C—B bond, the peaks at 1019 $cm^{-1}$and 896 cm^{-1} indicate for vinyl groups stretch in the case of FTIR spectrum of P(VPBA/HEMA/PEG-DA) membrane.

3.1.2. SEM investigation

The surface morphology of the membrane is an important factor. Fig. 2a and b demonstrates the SEM images of the glucose sensing membrane at different magnifications. As it could be seen from the SEM images, a homogenous and non-porous glucose membrane was obtained.

3.2. Spectral characterization studies

The binding process of phenylboronic acids with glucose diols is illustrated in Scheme 1. The fluorescence spectra were recorded at λ_{ex}= 211 nm and λ_{em}= 424 nm (Fig. 3.). The values of the fluorescence intensities of the membrane increased with increasing