Available online at www.sciencedirect.com

ScienceDirect

Procedia Engineering 168 (2016) 497 – 500

Procedia Engineering

www.elsevier.com/locate/procedia

30th Eurosensors Conference, EUROSENSORS 2016

Molecularly Imprinted Polymer-Carbon Nanotube based Cotinine sensor

Yawar Abbas*[1], Johan Bomer[1], Marjolein Brusse-Keizer[2], Kris Movig[2], Paul van der Valk[2], Marcel Pieterse[3], Loes Segerink[1], Wouter Olthuis[1], Albert van den Berg[1]

1. BIOS-Lab on a chip group, MESA+ Institute of Nanotechnology, MIRA Institute for Biomedical Technology and Technical Medicine, University of Twente, 7500 AE Enschede, The Netherlands
2. Medisch Spectrum Twente, Department of Pulmonary Medicine, Enschede, The Netherlands
3. Department of Psychology, Health and Technology, University of Twente, Enschede, The Netherlands

Abstract

A cotinine sensor based on the dc resistance of a polymer composite films is presented. The composite film comprises a cotinine selective molecularly imprinted polymer and carbon nanotube particles. This polymer film is deposited over a gold interdigitated electrode array to measure its electrical resistance. The electrical resistance of the imprinted polymer changes upon its selective binding to the cotinine molecule. The electrical resistance increases with the increase in cotinine concentration, for the addition of 1000 ng/ml cotinine the resistance increases by ca. 190 kΩ. As a control experiment the response of un-imprinted polymer is also tested, which does not show any dependence on the cotinine concentration. Cotinine concentration in body fluid reflects the extent of tobacco smoking. This sensor has a potential to be used to detect active and passive smoking levels.

Peer-review under responsibility of the organizing committee of the 30th Eurosensors Conference

Keywords: Cotinine measurement, molecularly imprinted -carbon nanotube polymer, conductance sensor

1. Introduction

Cotinine is one of the major metabolites of nicotine present in human body fluids (blood, saliva and urine) and has a half-life of 18-20 hrs. [1]. Therefore, cotinine can serve as a biomarker for tobacco exposure and its concentration in body fluid can be correlated to the extent of smoking. The concentration ranges of cotinine in urine of passive and active smokers (> 10 cigarette/day) are 1-100 ng/ml and > 650 ng/ml, respectively [1]. In laboratory practice, gas chromatography and high-performance liquid chromatography in combination with mass spectrometry are considered to be the gold standard for measuring cotinine [2]. These techniques are laborious, costly and multistep, limiting them

Peer-review under responsibility of the organizing committee of the 30th Eurosensors Conference
doi:10.1016/j.proeng.2016.11.236

only to research purposes. In clinic, a point of care (POC) device is inevitable which can measure the extend of tobacco exposure within a standard consultation time (ca. 20 mins).

Recently, there is a growing interest in impedemetric chemical sensors based on analyte-selective polymer film for POC clinical applications [3, 4]. This is due to their simple design, rapid response, cost effectiveness and better selectivity. These polymers can be tailored by molecular imprinting technique to make them selective to molecules of interest, therefore such polymers are called the molecularly imprinted polymer (MIP). The impedemetric sensing is achieved when such MIP is incorporated with carbon nano-tubes (CNT). The MIP enhances the selectivity to the molecule of interest due to physical or chemical affinity [3], whereas the CNT enhances the electrical properties (such as conductance) of the composite film [3].

We propose a cotinine sensor based on the dc resistance of MIPs-CNT composite polymer. A template of the cotinine molecule is created in the poly-4-vinylphenol (PVP) by first mixing the polymer with the cotinine and then dissolving the cotinine and then curing it. The MIP-CNT is deposited on a gold interdigitated electrode glass chip for electrical measurements. The chip along with the chemical cell is shown in figure 1d. The dc resistance of the MIP-CNT film is then tested in different cotinine concentrations. For control experiment, the un-imprinted polymer (without the templated features) film is also tested. This work shows the feasibility of a MIP-CNT based sensor to differentiate levels of cotinine between non-smoker, active and passive smokers.

2. Material and Methods

2.1. Inter-digitated electrode design

Interdigitated electrodes (IDEs) are fabricated to measure the dc resistance of the MIP-CNT film, where the polymer film is deposited over the IDEs. These electrodes were made of sputtered gold material on a glass substrate using the standard cleanroom processes, such as lithography and physical vapor deposition (PVD). The schematic of the cross-section of the chip is shown in figure 1a. Two different design of IDEs are tested in this work, IDE1 (number of fingers N = 60, width w = 40 µm, spacing s = 10 µm, length L = 4.45 mm and total area = 23 mm^2) and IDE2 (N = 82, w = 40 µm, s = 10 µm, L = 4.45 mm, and the total area = 46 mm^2). The cell contact for such dimensions of the planar IDEs is 1.25 cm^{-1} as reported in the theoretical calculation of the cell constant by Olthuis et al. 1995 [5]. The IDEs on the glass ship is shown in figure 1b.

2.2. Chemical and equipment

The single walled carbon nano-tube (SWNT), short 90% carbon basis with diameter × length 1-2 nm × 0.5-2 µm, cotinine analytical standard > 98.5% assay, poly-4-vinylphenol (PVP) with a molecular weight of ca. 11000, methanol solvent anhydrous 99.8% and toluene anhydrous 99.8% are all ordered from Sigma Aldrich, The Netherlands. Methanol is used as a solvent to dissolve PVP polymer and toluene is used as a templating solution to dissolve and extract cotinine. The electrolyte is composed of 0.5 M of KCl and NaCl background electrolyte and 0, 100 and 1000 ng/ml cotinine concentration. These levels are attributed to no smoking, passive and active smoking habit, respectively. A digital multimeter from Keithley 2000/E series is used to measure the resistance which is the sensor response. Moreover, an in-house built Teflon chemical cell is designed to connect the glass chip and perform experiment, see figure 1d.

2.3. Preparation of MIP-CNT film

The scheme for the preparation of the MIP-CNT based cotinine sensor is shown in figure 2. There are two main steps of preparation; (1) preparation of MIP-CNT polymer mix, (2) deposition of MIP-CNT film on the IDE chip. In the first step, a 20% w/v PVP and 1% w/v of CNT (SWNT) is dissolved in methanol solvent. This mixture serves as an um-imprinted polymer composite. To imprint it with cotinine molecule, a 1000 ng/ml cotinine solution is mixed with the PVP-CNT mixture. All the mixtures are then stirred overnight by a vortex mixer, giving a homogeneous suspension of CNT in the polymer matrix. In the second step, the MIP-CNT mixture is deposited on the gold inter-digitated electrode (IDE) array on a glass chip. First, the IDE electrode surface is activated by a plasma treatment.

Then a thin layer of the prepared polymer mixture is deposited over the IDE by pouring ca. 2 µl on the IDEs and let it dry for ca. 5 hrs. In the case of imprinted mixture, the cotinine molecules need to be extracted in toluene for 1 hr. The final sensor chip is shown in figure 1c.

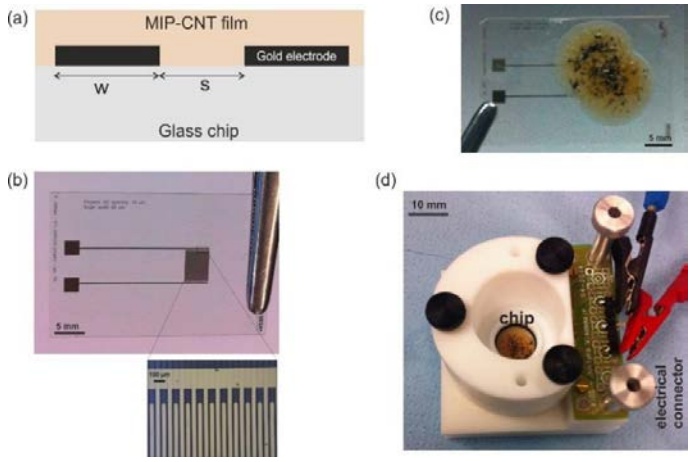

Figure 1: (a) Schematic of the cross-section of the IDE chip, w = width of planar electrode and s = spacing between electrodes (b) The top view of the gold IDEs on a glass chip and the magnified view of its fingers (c) The top view of the cotinine MIP-CNT polymer film deposited on the IDE chip (d) Snapshot of the sensor chip placed in a Teflon chemical cell with electrical connections.

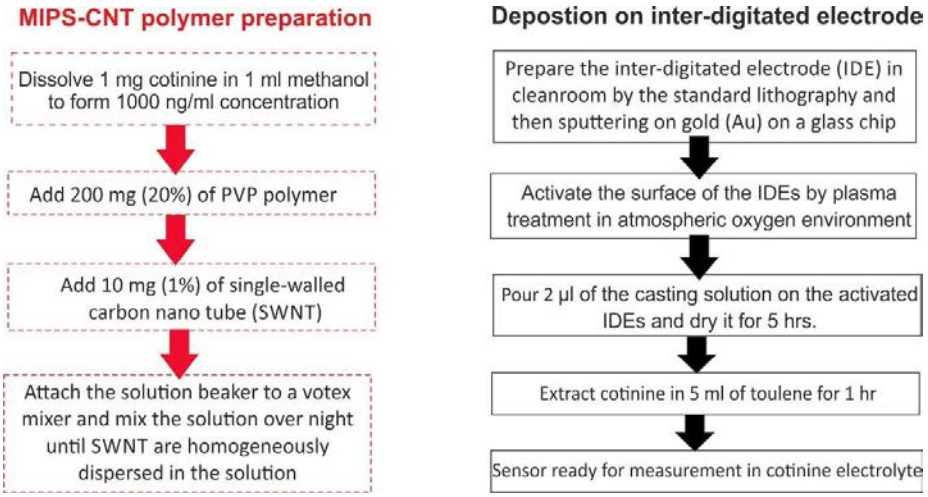

Figure 2: Scheme of the preparation of cotinine selective MIP and its deposition on the gold inter-digitated electrode array.

3. Results and discussion

The responses of the un-imprinted and imprinted polymer sensor are recorded for the control experiment. The response is shown in figure 3a The IDE1 sensor design is used in this experiment. In case of un-imprinted sensor there is no effect of cotinine concentration on the response since there is no template of cotinine. In comparison, the imprinted sensor shows an increase in the resistance with the increase in the cotinine concentration. This is due to the fact that the CNT are p-type structures (holes) and π-electrons from the aromatic ring of cotinine neutralize the holes in the CNT, resulting in the increase of its resistance. The change in the electrical resistance of the imprinted polymer is ca. 3 times (in case of 1000 ng/ml) higher than the control (i.e. un-imprinted polymer).

Moreover, to observe the effect of sensor dimensions, two different IDEs design were tested IDE1 and IDE2 with sensing area 23 and 46 mm^2, respectively. The response of these two designs for various cotinine concentration is shown in figure 3b. Both of these sensors have imprinted polymer. Due to its smaller surface area IDE1 has higher response (resistance) as compare to IDE2. For practical consideration it is good to have small surface area to avoid in-homogeneity of the MIP-CNT film. Moreover, in both the cases the change in response is higher from when changing from no cotinine to 100 ng/ml cotinine as compare to changing from 100 to 1000 ng/ml. This is due to the fact that fewer templated sites are available at the polymer surface as the templated sites are saturated in case of higher concentrations.

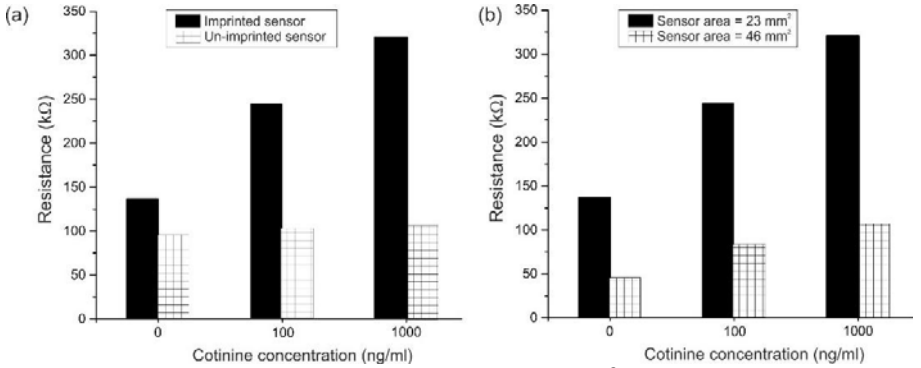

Figure 3: (a) Control experiment for an un-imprinted polymer film with IDE of 23 mm^2 (IDE1) surface area. The dc resistance of the un-imprinted polymer is measured for various concentration of cotinine (b) Sensor response of the cotinine imprinted MIP-CNT polymer film for various concentration of cotinine with IDEs of 23 mm^2 and 46 mm^2 surface area.

4. Conclusion

A conductive polymeric composite comprising poly-4-vinlyphenol polymer film and carbon nano-tubes can be used to detect the cotinine levels in electrolyte. The designed MIP-CNT film is selective to cotinine molecules. The dc resistance of the MIP-CNT polymer increases with the increase in cotinine concentration as the cotinine molecules bind to the templated sites of the polymer. A change in the resistance of 190 kΩ is observed when the cotinine concentration changes from 0 to 1000 ng/ml. The response of the un-imprinted polymer, as a control experiment, does show any change to the addition of cotinine. Moreover, the MIP-CNT film with higher surface area (46 mm^2) shows lower response as compare to the sensor with surface area of 23 mm^2. The tested cotinine levels showed that the sensor can distinguish between no, passive and active smoking levels.

Acknowledgements

This work is funded by through Pioneers in healthcare innovation vouchers from the Medical Spectrum Twente, the Twente Hospital Group and the University of Twente project partners. We would like to thank them all.

References

[1] P. Dhar, Measuring tobacco smoke exposure: quantifying nicotine/cotinine concentration in biological samples by colorimetry, chromatography and immunoassay methods, Journal of pharmaceutical and biomedical analysis, 35(2004) 155-68.

[2] D. Best, E.M. Green, J.H. Smith, D.C. Perry, Dipstick tests for secondhand smoke exposure, Nicotine & Tobacco Research, 12(2010) 551-6.

[3] S. Antwi‐Boampong, K.S. Mani, J. Carlan, J.J. BelBruno, A selective molecularly imprinted polymer‐carbon nanotube sensor for cotinine sensing, Journal of Molecular Recognition, 27(2014) 57-63.

[4] E. Pardieu, H. Cheap, C. Vedrine, M. Lazerges, Y. Lattach, F. Garnier, et al., Molecularly imprinted conducting polymer based electrochemical sensor for detection of atrazine, Analytica Chimica Acta, 649(2009) 236-45.

[5] W. Olthuis, W. Streekstra, P. Bergveld, Theoretical and experimental determination of cell constants of planar-interdigitated electrolyte conductivity sensors, Sensors and Actuators B: Chemical, 24(1995) 252-6.