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MIP-based Sensors for Fast Nicotine Monitoring in Aerosol

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Summary:

Nicotine is the main active component of tobacco. Its quantification in aerosols and particularly the amount delivered in lungs is of great interest to track its impact on health. Current detection methods rely on the use of mass spectroscopy coupled with liquid chromatography. However, this requires highly qualified personnel and expensive equipment. In this context, we demonstrated that Molecular Imprinted Polymers (MIP) as sensing layer deposited on electrodes are very efficient to allow fast and cheaper quantification of nicotine in aerosols.

Keywords: Molecularly imprinted polymers, nicotine detection, electrochemical sensors, fast response

Inhalation toxicological investigations and the development and pre-clinical testing of inhalable drugs require assessing the deposition kinetics of aerosol constituents on the epithelia of the respiratory tract or on in vitro models. A common in vitro approach is the deposition of the test aerosol on a trapping surface under controlled conditions, followed by quantification of deposited individual targeted aerosol constituents. This requires highly sensitive and selective analytical methodologies such as coupled chromatography - mass spectrometry, needing highly qualified personnel and expensive equipment and are not easily accessible. In this context, a promising technology for the quantification of aerosol deposition are chemically selective sensors and among them, molecularly imprinted polymers (MIP) showed very interesting abilities to selectively concentrate the target molecule for a better read-out. Matsui [1] reported one of the first nicotine MIPs in 1996. Nicotine MIPs were firstly used to preconcentrate nicotine before chromatography analysis [2] but quickly, attention turned on the analysis of cigarette smokes [3]. They also had interest for the delivery of nicotine through patches. Sensors were also developed for the analysis of residues in urines [4]. Finally, regarding detection methods, besides QCM [5], capacitive measurement [6] and optical detection [7] were used. No MIP for electrochemical detection of nicotine was mentioned. In this work, MIP were combined with electrochemical chips to build the nicotine sensors. Two approaches were evaluated: UV-curing of MIP on the electrode and electrodeposition.

MIP-based sensors are usually built by depositing preformed nanoparticles of MIP, but this leads to rather thick layers. We therefore focused on a polymer-based MIP formulation deposited as a thin film on the electrode and cured by UV exposure. The formulation is based on divinylbenzene and methacrylic acid, dicumyl peroxide being the activator of polymerization. Despite the polymer layer is insulating, we managed to deposit a very thin film (few 10ths of nanometers) to ensure sufficient recorded signal by using Pico-Pulse Jetting.

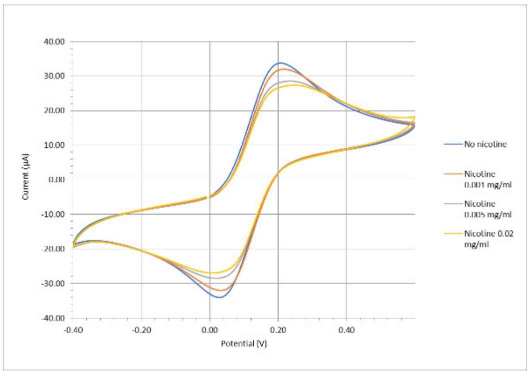

Fig. 1: detection of nicotine by MIP deposited by Pico-Pulse Jetting on working electrode of screen-printed carbon electrodes with Ag/AgCl reference.

MIP-based nicotine sensors were thus printed and further characterized. Direct monitoring of nicotine at its rather high redox potential was found to damage the sensing layer. Therefore, an indirect electrochemical measurement was developed using Fe(II)/Fe(III) as probe, avoiding high potential and deterioration of the MIP layer. This Fe(II)/Fe(III) potential value is directly linked to the presence of Nicotine and Fig. 1 shows an example of nicotine detection with this approach.

For such kind of sensors, calibration is then needed, and Fig. 2 shows a calibration curve obtained with our sensor over the nicotine concentration range of interest.

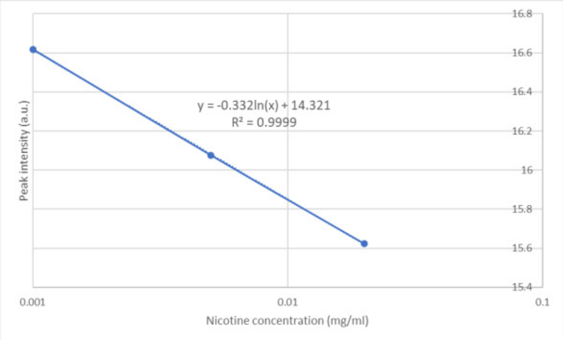

Fig. 2: calibration of MIP-based nicotine sensors fabricated by Pico-Pulse Jetting

Finally, we also investigated its sensitivity, its selectivity, and its stability. Very low amounts of nicotine (down to few ng/ml) were detectable in short times (10-15 min) allowing straightforward and fast measurements. The selectivity was very high even in presence of nicotine metabolites such as cotinine (Fig. 3). The sensor was exposed to various pH, solvents and biological media conditions and showed sufficient reliability for the foreseen application.

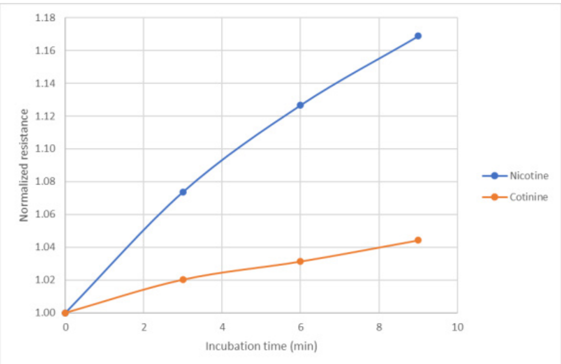

Fig. 3: selectivity of the MIP-based sensor fabricated by Pico-Pulse Jetting

Due to some limitations with in-situ UV-curing, we also studied MIP electrodeposition. For this purpose, we developed formulations and methods to reproducibly deposit MIP layers on electrodes by electrochemistry. Compared to standard MIP bulk-synthesis, this approach required the use of new electropolymerizable monomers such as aniline, pyrrole or thiophene. Several parameters allow a fine control on the created electrografted layer. The number of grafting cycles impacts the growth of the layer whereas the potential window used controls eventual cross-linking of the layer.

Formulations were then refined to increase the sensitivity and the selectivity by incorporating co-monomers such as acrylic acid or methyl acrylate. Those functional monomers promote more specific interactions with the target molecule nicotine which, in theory, enhances the selectivity. We were thus able to reach a very high sensitivity (in nanomolar/ppb range) together with keeping short analysis times (typically 3 to 5 minutes) and high selectivity.

We thus developed nicotine electrochemical sensors allowing fast and precise determination of nicotine in solution. Performances and robustness were optimized to achieve on-line measurement of nicotine levels in aerosols.

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