

A Non-Invasive Biosensor for Albumin Detection in Tear Fluid Based on Molecularly Imprinted Polymers

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Summary:

Tears are biomarker-rich biofluids enabling non-invasive monitoring of disease progression. We present a molecularly imprinted polypyrrole electrochemical sensor for albumin detection, targeting future integration into contact lenses for ocular inflammation monitoring. Sensor performance was evaluated in simulated tear fluid prepared in phosphate-buffered saline. High selectivity was observed against major interferents. The sensor achieved a detection limit of 0.154 mg/L and a 76.77% recovery rate, indicating effective regeneration and suitability for reusable, tear-based healthcare monitoring applications.

Keywords: biosensors, tears, albumin, molecularly imprinted polymers (MIPs), diagnostics.

Background, Motivation and Objective

Albumin concentration in tears ranges from 10 to 200 $\mu\text{g/ml}$ [1], with increased ocular levels potentially indicating vascular leakage across the ocular tear-blood barrier, offering an opportunity as a biomarker of ocular inflammation and an indicator of ocular integrity [2]. Conventionally, albumin concentrations are measured using bulk methods such as liquid chromatography-mass spectrometry (LC-MS) and high-performance liquid chromatography (HPLC), enzyme-linked immunosorbent assays (ELISA), radioimmunoassay, turbidimetry, and nephelometry. These methods require lengthy sample preparation and sometimes large instruments, which limit their applications beyond lab environments [3]. Integration of sensing platforms into contact-lens-based detection offers the advantages of minimal invasiveness, potential for continuous monitoring, and remote applications, and addresses the challenges of bulkiness and sample preparation [4]. Furthermore, molecularly imprinted polymers' (MIPs) ability to act as biomimetics that imitate the antigen-antibody interaction in biosensing applications opens up opportunities for biomarker monitoring [5].

The objective of this study was to develop a proof-of-concept sensor protocol for the detection of human serum albumin in tear fluid using molecularly imprinted polymers (MIPs), with the aim of future integration into contact lens-based biosensing applications.

This was accomplished through the fabrication of a polypyrrole MIP electrochemical sensor on

a carbon screen-printed electrode, followed by optimisation of albumin sensitivity and selectivity and testing under simulated tear fluid conditions.

Description of the New Method or System

The electrochemical sensor was prepared by running 7 scans of a solution containing 100 mg/L albumin in 1X PBS buffer and pyrrole on a carbon screen-printed electrode over the potential range -0.2V to +0.8V at a scan rate of 50 mV/s using a PalmSens 4 potentiostat. The buffer acted as an electrolyte, with the applied potential oxidising pyrrole to produce radical cations that initiated the chain reaction leading to polypyrrole MIP. To create the MIP, sodium hydroxide (NaOH) was used to disrupt the albumin bonds in the polymer, with sodium chloride (NaCl) to adjust the ionic strength for effective removal. Cyclic voltammetry was then performed to evaluate the performance of the MIP sensor, and simulated tears containing interferents were used for selectivity studies.

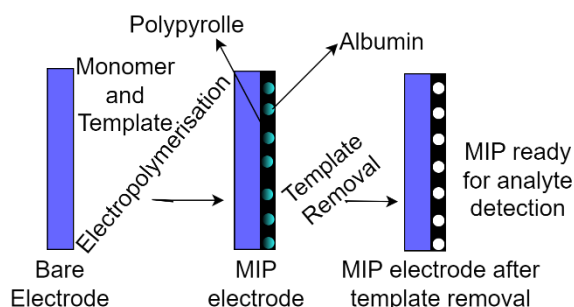


Fig. 1. Schematic representation of the molecularly imprinted polypyrrole electrochemical sensor fabrication for albumin concentration detection.

Results

The measured peak currents during rebinding of the prepared MIP showed an inverse relationship with human serum albumin concentration. An increase in albumin concentration decreased peak currents, with higher concentrations indicating MIP saturation, as shown in Figure 2.

The developed MIP achieved a 450% binding capacity compared to 84.06% for the non-imprinted (NIP), indicating selective binding to the target analyte by the MIP.

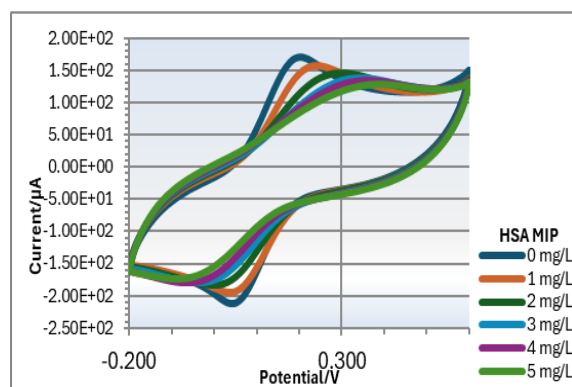


Fig. 2. Cyclic voltammetry rebinding curves recorded at albumin concentrations of 0–5 mg/L, showing a progressive decrease in peak currents with increasing albumin concentration

A recovery attempt of the MIP achieved a 76.77% recovery. This was achieved by washing the rebinded analyte with NaOH, NaCl, and H₂SO₄, then performing a cyclic voltammetry scan and comparing it with the first wash performed during MIP development.

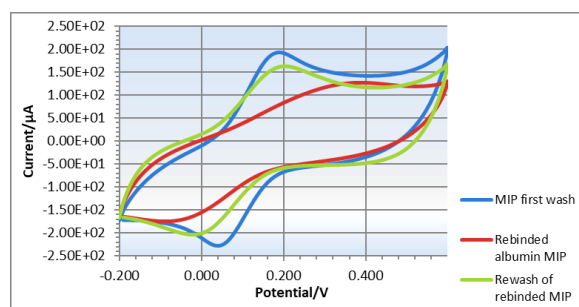


Fig. 3. Recovery experiments of the MIP sensor evaluating reusability, showing a recovery rate of 76.77%.

Further studies were carried out using simulated tears and the principal tear proteins as interferents to assess selectivity. Secretory IgA, lysozyme, lactoferrin, and albumin solutions were prepared in 1X PBS at the tear concentration levels, and dropcast on the MIP on a SPE. The results showed an imprinting factor of 1.74

for albumin, compared to 0.36, 0.4, and 0.29 for lysozyme, IgA, and lactoferrin, respectively.

Potential and Clinical Relevance

The MIP demonstrates significant potential as an electrochemical sensor for integration into wearable platforms for albumin concentration monitoring, particularly in tear fluid. Advances in microelectronics and microelectrode fabrication have enabled increasing miniaturisation, paving the way for lab-on-a-chip and smart sensing applications. This work represents an initial step in the development process; future studies should focus on further reducing non-specific binding and mitigating biofouling to enable reliable performance in in vivo applications.

Conclusion

A polypyrrole electrochemical sensor was developed and tested in buffer and simulated tear fluid, achieving detection and quantification limits of 0.154 mg/L and 0.466 mg/L, respectively. The biocompatibility and high conductivity of polypyrrole make it an attractive material for biosensor development targeting albumin and other diagnostic analytes.

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