Hydrogel Whispering-gallery Mode Microresonators for Toxic Heavy Metals Detection in Chinese Herbals

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ABSTRACT

Trace detection of heavy metal ions in herbal extracts is essential for ensuring the safety and regulatory compliance of Chinese herbal medicine (CHM). Hydrogels, as a class of promising sensors, exhibit exceptional ion absorption capability and adaptability. However, conventional hydrogel-based sensors are prone to be variable in perception, suffering from limited sensitivity and low signal-to-noise ratios, especially in fluorescence-based detection schemes. Herein, we propose a hydrogel-based optofluidic microcavity sensor that integrates aptamer-functionalized hydrogel films within a whispering-gallery-mode (WGM) microresonator, enabling it to amplify subtle signals while simultaneously analyze in chemically complex environments. The specific binding between target metal ions and aptamers induces local shrinkage of the hydrogel network, leading to a refractive index (RI) change that manifest as a red shift in the WGM resonant wavelength. This optical transduction strategy significantly enhances both sensitivity and selectivity compared to conventional platforms. Finally, experimental validation with Pb^{2+} and Hg^{2+} demonstrates the robust sensing performance of the system, with detection down to nanomolar levels, highlighting its potential for practical trace analysis. Our functional hydrogel optofluidic sensor offers a novel and effective approach for heavy metal ion detection in CHMs.

Keywords: hydrogel, whispering-gallery mode, heavy metal ion detection, optofluidic, aptamer-cross-linked

1. INTRODUCTION

Chinese herbals play critical roles in treating diseases. For instance, the discovery of artemisinin won the Nobel Prize for its treatment in malaria [1, 2]. Based on the great importance and potential that Chinese herbals show, it is essential to ensure their safety. However, Chinese herbals tend to contaminate with toxic heavy metals like Pb^{2+} and Hg^{2+}, which poses significant safety that concerns to health since they are bioaccumulated. To address these risks, many countries have established strict standards to limit heavy metal content in Chinese herbals. Ensuring compliance with these standards necessitates highly sensitive and specific detection methods.

Conventional detection techniques have limitations in real application. Inductively coupled plasma–mass spectrometry, known as ICP-MS [3, 4], atomic absorption spectrometry [5, 6] and atomic fluorescence spectrometry [7] offer excellent sensitivity and enable quantitative analysis. However, these methods are often limited by high costs, complex equipment and time-consuming procedures [8]. Meanwhile, hydrogels have emerged as promising materials for heavy metal detection due to their unique structures. However, most of existed hydrogel-based methods highly rely on naked-eye observation [9, 10, 11] or fluorescence detection [12-16]. The former tends to be subjective, and the results may vary

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from person to person; in the meantime, the latter often suffers from broad emission spectra and low signal-to-noise ratios (SNR), making it difficult to capture subtle signals in complex extraction solutions [17, 18].

To overcome these limitations, we proposed a hydrogel optofluidic microcavity sensor, and the sensing mechanism was illustrated in Figure 1a. The sensing platform integrated the hydrogel film within a whispering-gallery mode (WGM) resonator, making it feasible to amplify subtle analyte signals through strong light–matter interaction. As shown in Figure 1b, the newly formed conformations in the sensor led to changes in the refractive index (RI), manifesting as a measurable shift in red-wavelength. Through monitoring the spectral shift, the concentration of targeted heavy metal ion could be accurately analyzed. The thickness of hydrogel was further evaluated to optimize the sensitivity and selectivity. Finally, this platform was tested for Pb^{2+} and Hg^{2+} detection and applied to Chinese herbal samples, demonstrating its high sensitivity and the possibility of application in the real world.

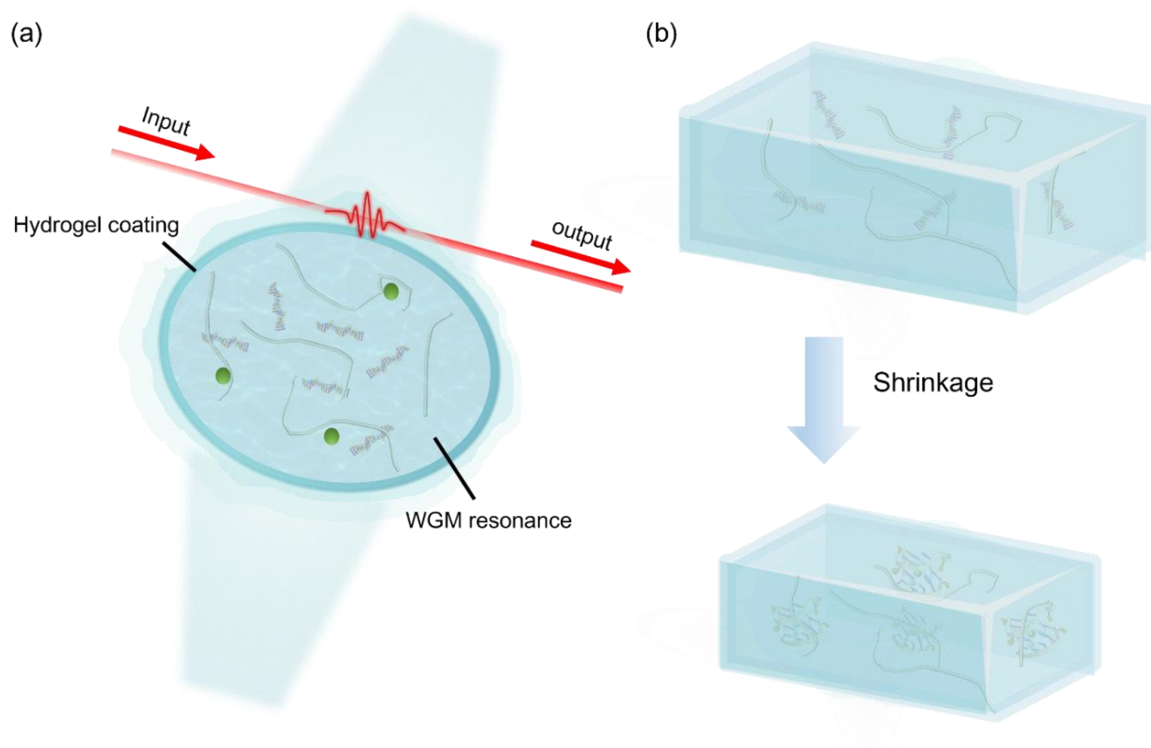

Figure 1. Principle of the hydrogel optofluidic microcavity for heavy metal ion detection. (a) The sensing mechanism. (b) When encountering heavy metal ions, the aptamer structure was changed, inducing hydrogel shrinkage and RI alteration.

2. RESULTS AND DISCUSSIONS

The hydrogel optofluidic microcavity was achieved on a microbubble WGM cavity with hydrogel coating. The WGM served as a transduction method, while simultaneously, a fiber taper was used to couple the evanescent field. To obtain high sensitivity for detecting heavy metal ions, the hydrogel was decorated with aptamers. When encountering the target metal ions, such as Pb^{2+} and Hg^{2+}, conformational changes occurred within the aptamer structure, and the binding event induced localized shrinkage of the hydrogel network, thus leading to an alteration in RI, especially in regions that influenced by strong evanescent fields.

As presented in Figure 2a, we utilized a tunable laser as light source to excite the WGM within the hydrogel optofluidic microcavity, while simultaneously, a powermeter was employed to record the optical signal. The RI change caused by hydrogel shrinkage manifested as a measurable red shift in the WGM resonant wavelength. To further explore the relationship between RI and hydrogel shrinkage, we used NaCl solutions with various concentration to simulate. The transmission spectra with corresponding wavelength under different RI environments was illustrated in Figure 2b, from which an obvious red wavelength shift could be observed. As established in Figure 2c, the relationship between the resonant wavelength shift and RI was linear, allowing for quantitative analysis of heavy metal ion concentrations in the solution.

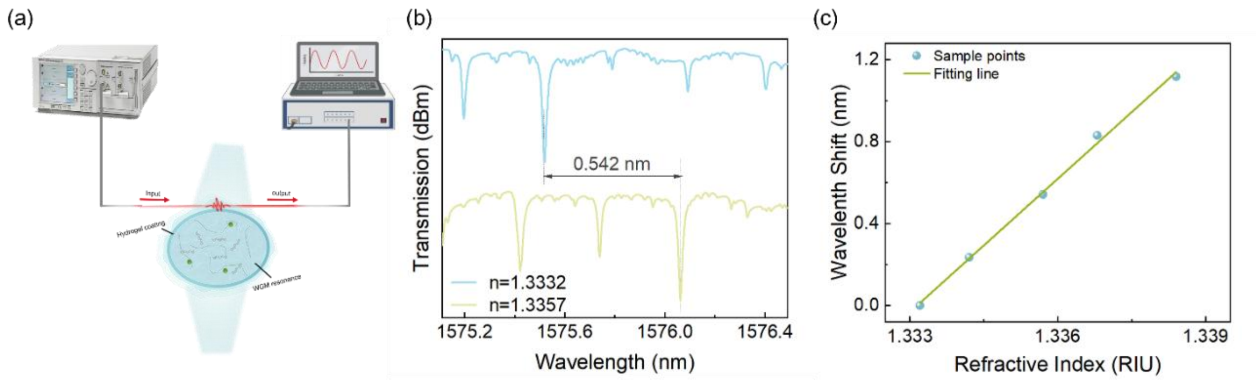

Figure 2. (a) The sensing platform, equipped with a tunable laser as the light source, and a powermeter to capture the optical signal. (b) The transmission spectra and its corresponding wavelength under various RI. (c) Fitting lines showed the linear relationship between RI and wavelength shift.

To optimize the sensitivity and selectivity for heavy metal ion detection, the effect of hydrogel thickness was further evaluated. We systematically varied the hydrogel thickness and measured the corresponding spectral shifts in response to a fixed concentration of Pb^{2+} ions (300 nM). As shown in Figure 3, thicker hydrogel layers tended to restore more energy, and the light-matter interactions within the microcavity were enhanced, resulting in smaller spectral shifts for the same ion concentration. Meanwhile, we found that thicker hydrogel coating resulted in a long time for the shift to be stabilized. Our experiments identified an optimal hydrogel thickness of 0.79 μm, which provided a balance between sensitivity and response time.

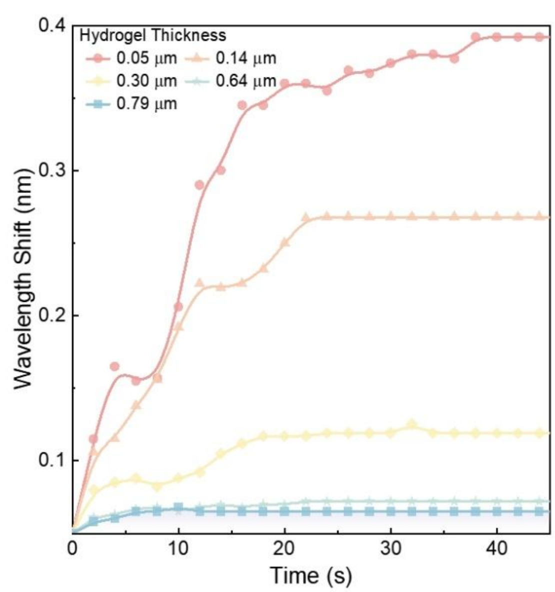

Figure 3. The response time and wavelength shift under various hydrogel thickness in the 300 nM Pb^{2+} solution.

The sensing performance of the hydrogel optofluidic microcavity for detecting Pb^{2+} and Hg^{2+} were rigorously tested. Figure 4a illustrated the response observed at a concentration range of 10–300 nM for Pb^{2+}, with a correlation coefficient

(R^2) of 99.71% for the fitting line. Similarly, we changed the aptamer as Hg^{2+} responsive one, and integrated it within the platform. As shown in Figure 4b, Hg^{2+} detection yielded comparable sensitivity, which further underscored the versatility of the aptamer-functionalized hydrogel microcavity. These results affirmed the capability to detect heavy metal ions at trace levels, making it suitable for real-world applications in monitoring the safety of Chinese herbals.

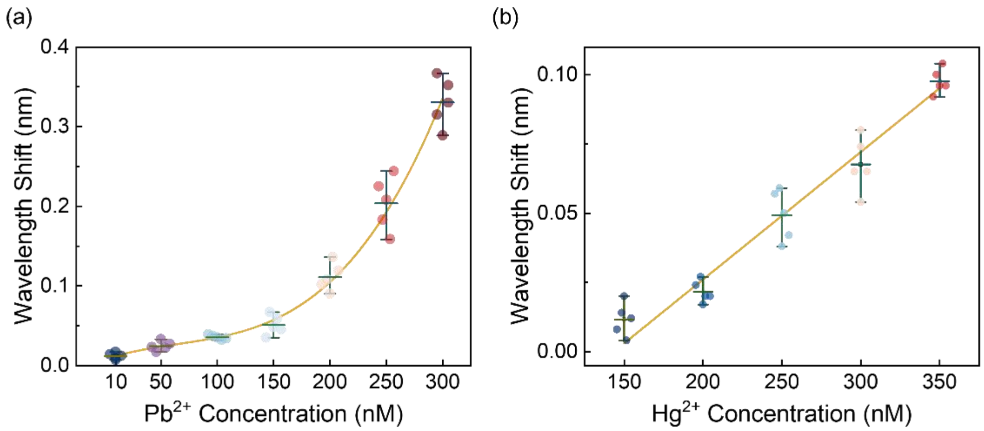

Figure 4. Wavelength shifts caused by various concentrations of heavy metal ions. (a) A range of 10–300 nM Pb^{2+}. (b) A range of 150–350 nM Hg^{2+}.

To verify the specificity of the sensing platform, we utilized the platform to test the response to various interfering ions, such as Mg^{2+}, Cu^{2+} and Ca^{2+}, at concentrations that could potentially be presented in Chinese herbals. As shown in Figure 5, the sensor demonstrated high specificity for Pb^{2+}, with negligible interference from other ions.

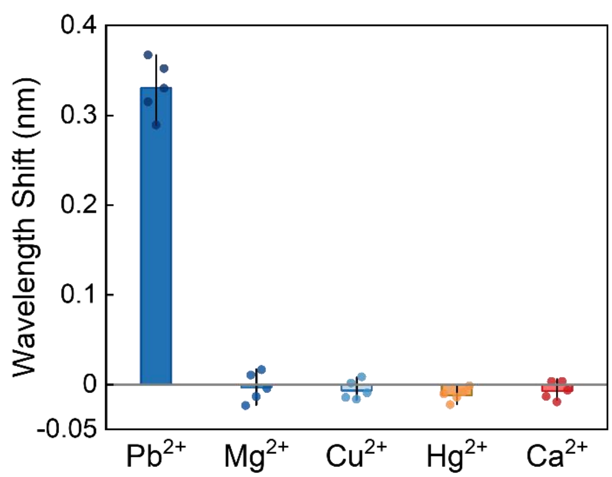

Figure 5. Wavelength shift for detecting other heavy metal ions under the sensing platform with Pb^{2+} aptamer.

In addition, the practical applicability of the hydrogel sensor was further demonstrated through its application to five different Chinese herbals samples. The concentrations of Pb^{2+} and Hg^{2+} detected by the hydrogel optofluidic microcavity sensor were compared with results obtained from conventional methods. The correlation between the different methods was strong, with relative errors below 5%, confirming the accuracy of the hydrogel sensor.

3. CONCLUSIONS

In this work, we developed a hydrogel-based WGM microcavity sensor, which represented a significant advancement in the detection of heavy metal ions. The sensing platform was achieved through strong light-matter interaction, which could influence the RI of the hydrogel and changed its conformation, leading to a measurable wavelength shift. Then, we demonstrated the concentration of heavy metal ions could be evaluated by the value of the shift. The sensor has been proved to have high sensitivity, specificity and reusability, making it a promising tool. Future research will focus on finding the balance between compact size and sensitivity of the sensor, through further optimizing the thickness of both hydrogel film and silica. We regarded this platform can be applied in other situations, like environmental monitoring and the detection of toxic materials.

4. ACKNOWLEDGMENTS

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