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PEGylated Lipopolymer-based Biosensor for Lung Cancer Biomarker Detection: Bridging Environmental Mentoring for Health Diagnostics

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KEYWORDS

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ABSTRACT

This work investigates the fabrication of a functionalized PEGylated lipopolymer sensing film on a quartz crystal microbalance (QCM) with a fundamental frequency of 30 MHz AT-cut gold electrode for the detection of lung cancer biomarkers using four types of volatile organic compounds (VOCs), namely propanol, decane, hexanal, and ethyl benzene, within a concentration range of 50 ppm to 1 ppm. The QCM sensors coated with PEG, Lipo-M, and Lipo-P were able to detect the biomarkers decane and ethyl benzene, with the lowest detectable concentration being 4 ppm. In contrast, for detecting hexanal and 1-propanol, the sensor coated with Lipo-P exhibited the highest sensitivity, detecting concentrations as low as 8 ppm and 7 ppm, respectively. This fabrication of sensing material on the QCM not only demonstrated higher sensitivity in VOC detection but also enhanced the selectivity of the sensor toward detecting lung cancer biomarkers.

1. INTRODUCTION

Lung cancer is one of the leading causes of cancer-related deaths worldwide, with an estimated 1.8 million fatalities reported in 2022 [1]. According to the Ministry of Health's most recent Malaysia National Cancer Registry Report, published in July 2024, lung cancer is the third most commonly diagnosed cancer in Malaysia, following breast and colorectal cancers. The incidence rate increased from 9.8% during 2012–2016 to 10.1% during 2017–2021 [2]. In Malaysia, 16.0% of cases were diagnosed in men, while 13.7% were reported in women [2].

Lung cancer can result from smoking [3] and prolonged exposure to volatile organic compounds (VOCs) [4], which are commonly present in everyday products such as automotive fluids, paint thinners, coal, air fresheners, gasoline, and diesel exhaust [5]. Early detection of lung cancer is essential for improving patient survival rates. A widely accepted approach involves analyzing the types and concentrations of VOCs in the exhaled breath of cancer patients [6]. This method enables quicker diagnosis, allowing for timely and effective treatment.

Electronic nose (e-nose) devices are widely used for detecting volatile organic compounds (VOCs) [7]. Among these, the quartz crystal microbalance (QCM) is one of the most extensively studied e-nose technologies by researchers. By using a sensing material applied as a coating on the sensor surface, the QCM can detect volatile compounds with high sensitivity and remarkable selectivity [8], [9]. When VOCs interacts with the sensor surface, the coated polymer serves as an active site, facilitating interactions between ions in the gas molecules and the polymer film. This mechanism enhances the sensor's overall sensitivity.

In a previous study, we reported that QCM sensors fabricated with succinyl, carboxyl, and lipid coatings could successfully detect decane, ethyl benzene, hexanal, and 1-propanol [10], [11]. In this study, we explore the use of a different type of polymer to evaluate the sensitivity of QCM sensors when doped with these materials and to determine the detection limits.

2. EXPERIMENTAL PROCEDURE

2.1 Materials and Reagents

The reagents used in this study included analytical-grade of polyethylene glycol (PEG) with molecular weight of 2000, functionalized PEGylated lipopolymer 1,2-distearoyl-sn-glycero-3-phosphoethanol-amine-N-[methoxy (PEG) 2000] (Lipo-M) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[3-(2-pyridyldithio) propionate (PEG) 2000] (Lipo-P). These reagents were purchased from Avanti Polar Lipids, Alabama, and used without further purification. The volatile organic compounds utilized in the study included 1-propanol (C_3H_8O), decane ($C_{10}H_{22}$), ethyl benzene (C_8H_{10}), and hexanal ($C_6H_{12}O$), all of which were purchased from Merck, United States, and used without further purification.

2.2 Preparation of Sensing Film

Approximately 2 mg of sensing material was added to a clear glass vial, heated at 30 ℃ for 60 seconds to induce melting, and then 2 mL of chloroform was added. The mixture was continuously shaken to obtain a homogeneous solution.

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2.3 Deposition of Sensing Film onto QCM Sensor

Approximately 2 μL of ethanolic polymer solution was applied to the center of both sides of a 30 MHz AT-cut QCM with a gold electrode using a micropipette. The coated sensor was then dried under ambient air in a covered petri dish in a fume hood for 24 hours before the gas fabrication process, leaving a thin film deposited on the surface of the quartz crystal.

2.4 Detection of Biomarker Using QCM Sensor

The experimental setup is illustrated in Figure 1. The QCM sensor was installed in an oscillator circuit inside a desiccator and purged with ambient air using an air pump system at a consistent flow rate of 600 mL min^{-1} for 15 minutes to establish a stable baseline. VOCs were transferred into a gas bottle at an initial concentration ranging from 1 to 50 ppm, and air was allowed to flow into the gas bottle for 300 seconds to facilitate vaporization. The sensor was then exposed to the vaporized VOC for 180 seconds before the airflow into the desiccator was cut off. The sensor was monitored for up to 700 seconds, and the readings were recorded for further analysis.

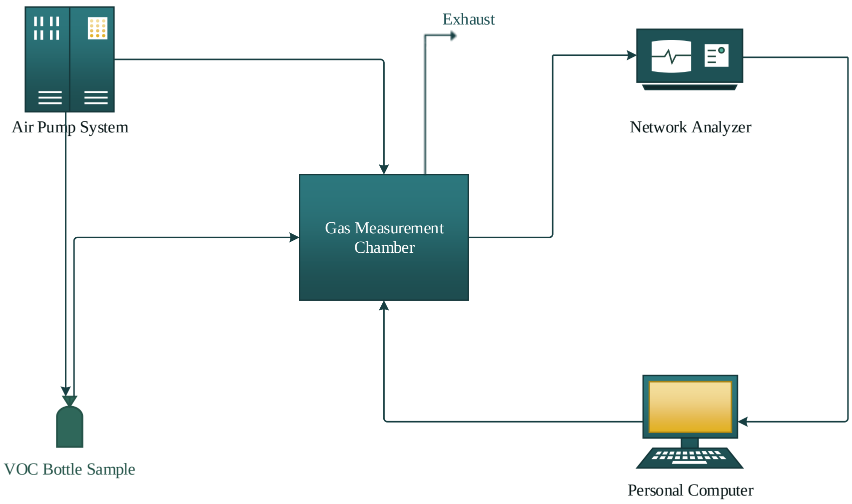

Figure 1. Schematic diagram of measurement setup to conduct experiment on detection of VOC using QCM in this work.

3. RESULTS AND DISCUSSION

3.1 Evaluation on Detection Limit by QCM

In detecting the detection limit for biomarker exposure using QCM, the lower the concentration of the biomarker that the sensor can detect, the better its detection capability. The sensor is considered sensitive if it can respond to the smallest presence of the biomarker. The properties of the sensing films after exposure to the biomarker are summarized in Table 1. According to the data, all sensors were able to detect the biomarker at initial concentrations ranging from 10 to 50 ppm. However, as the concentration was reduced further, the sensitivity began to change. Based on the observations, the lowest concentration of biomarker detectable by the three sensors was decane and ethyl benzene, which were detected as low as 4 ppm.

In contrast, exposure to hexanal showed that Lipo-M and PEG could detect it down to 9 ppm, while Lipo-P detected it at 8 ppm. In comparison, for 1-propanol, Lipo-M detected as low as 8 ppm, while Lipo-P and PEG detected it at 7 ppm. Overall, coated sensors showed greater selectivity towards non-polar compounds (decane and ethyl benzene) compared to polar compounds (1-propanol and hexanal). This is because non-polar compounds have a greater tendency to dissolve in non-polar environments, driven by stronger interactions through van der Waals forces and hydrophobic interactions, leading to enhanced detection by the QCM sensor.

Table 1 Detection limit of coated sensors when exposed to biomarker within 1 ppm to 50 ppm

VOCs	Lipo-M	Lipo-P	PEG
1-Propanol	8 ppm	7 ppm	7 ppm
Decane	4 ppm	4 ppm	4 ppm
Ethyl benzene	4 ppm	4 ppm	4 ppm
Hexanal	9 ppm	8 ppm	9 ppm

4. CONCLUSION

The sensors coated with functionalized lipopolymer compounds were able to detect VOCs at much lower concentrations. Sensor coated with PEG, Lipo-M and Lipo-P were found to be more effective at detecting decane and ethyl benzene, with the lowest detectable concentration being 4 ppm. Detection of 1-propanol and hexanal was achieved at minimum concentrations of 7 ppm and 8 ppm, respectively, using Lipo-P. Therefore, QCM sensors coated with PEGylated lipopolymer have proven to be a successful design and application in health diagnostics by effectively detecting VOCs.

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