Experimental Evaluation and Modeling of Adsorption Phenomena of Nanoliposomes on Poly(dimethylsiloxane) Surfaces

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Nanoparticles, such as exosomes or liposomes, have been widely studied using poly(dimethylsiloxane) (PDMS) microchannels. The interaction between nanoparticles and solid surfaces is an important subject for basic and applied research on nanoparticles, but there have been few reports on the use of microchannels for this purpose. Micro-scale systems serve as a useful platform for adsorption analysis because of their large surface-to-volume ratio. In this study, we attempted to develop a platform to study the adsorption phenomena of nanoparticles on solid surfaces using a microchannel, in which a model that analyzes dynamic (i.e., non-equilibrium) adsorption was used. This model allowed quantitative analysis of nanoliposome adsorption onto the surface of a PDMS microchannel.

Keywords: Solid surface adsorption, Analytical model, Non-equilibrium adsorption, nanoliposome, PDMS microchannel

1. Introduction

Nanoparticles (NPs) such as exosomes and liposomes have been examined for their biomedical applications [1, 2], using poly(dimethylsiloxane) (PDMS) microchannels as a platform for analysis [3–5]. In the analysis, NPs can be characterized to obtain properties such as size and zeta potential, which provide important details for future applications [6–10].

Another property that is important for understanding the behavior of NPs is their interaction with solid surfaces [11]. Adsorption phenomena are crucial in many applications and studies involving NPs [12]. Moreover, adsorption depends on the properties of both NPs and solid surfaces; accordingly, there are different types of interactions, such as hydrophobic or electrostatic interactions [13, 14].

For adsorption analysis, a microchannel is a suitable setup as it is a micro-scale system that has a higher surface-to-volume ratio (S/V ratio) compared with macro-scale systems, which allows adsorption to be more easily observed [15, 16]. Quantitative analysis of the adsorption experiment data can be performed to understand the interactions between NPs and solid surfaces. Conventionally, adsorption models such as the Freundlich isotherm or Langmuir isotherm have been used to quantitatively measure the adsorption phenomena of particles [17–19]. These prove to be accurate in describing the rate of particle adsorption and are highly useful in applications involving the adsorption of NPs [20, 21]. However, one drawback is that these models typically require a longer observation time (such as one or two hours) to observe the NPs adsorb onto the adsorbents until an equilibrium state is reached. Moreover, multiple experiments with different initial NP concentrations...
are required to gather a range of data points to accurately measure the adsorption rate of these NPs, which involves expending more time.

In this study, we attempted to establish a platform for analyzing the adsorption of NPs on solid surfaces using a microchannel setup. The adsorption of nanoliposomes observed under light-sheet illumination was quantitatively analyzed using the experimental data reported in our previous study [13]. An adsorption model was developed to analyze the transient adsorption phase of the nanoliposomes on the PDMS surface under a shorter observation time. The functionality of this model was compared with that of traditional adsorption models.

2. Experimental

The nanoliposomes were prepared using the thin-film hydration method [10, 13]. An appropriate molar ratio of lipids and cholesterol was dissolved in chloroform and the lipid film was deposited on a vial by evaporating the solvent. Subsequently, the lipid film was hydrated with PBS buffer with pH 7.4 for 24 h and original liposomes were prepared. Prior to performing adsorption experiments, the original liposomes were extruded through a polycarbonate membrane with 100 nm pore size using an Avanti® mini-extruder to form nanoliposomes with around 100 nm in diameter. Three different liposomes were prepared using 1,2-dilauroyl-sn-glycero-3-phosphocholine (DLPC), 1,2-di-O-octadecenyl-3-trimethylammonium propane (chloride salt) (DOTMA), and L-α-phosphatidylserine (Brain, Porcine) (sodium salt) (PS). The molar ratios were DLPC and cholesterol at 4:1 for the DLPC liposomes, DOTMA and cholesterol at 1:1 for the DOTMA liposomes, and DLPC, PS, and cholesterol at 5.55:0.45:4 for the PS liposomes. The measured average size of DLPC, DOTMA, and PS nanoliposomes were 117.0 nm, 117.3 nm, and 111.7 nm, whereas the polydispersity indexes were 0.10, 0.08, and 0.08, respectively. The adsorption data of three different nanoliposomes in microchannels (200 μm width, 200 μm height, and 10 mm length,) were obtained from light-sheet illumination [13]. All three nanoliposomes were found to have particle numbers in the region of interest (ROI). DLPC and DOTMA nanoliposomes adsorbed onto the PDMS surface, while PS nanoliposomes were adsorbed onto the polyethyleneimine (PEI)-coated PDMS surface. A calibration curve to convert particle number in ROI (particles) into concentration (particles/mL) was obtained using polystyrene nanobeads (NIST particle size standard, 100 nm). Using the calibration curve (Fig. 1), the particle number in ROI was correlated with the particle concentration in the bulk sample.

3. Model

The adsorption data [13] decreased exponentially, and therefore, to set up the adsorption model, we analyzed the mass transfer of nanoliposomes as the concentration decays over time. This is similar to the integrated first-order rate law as shown in Equation 1 [22].

\[
\frac{dc}{dt} = -kC
\]  

(1)

Where \(C\) is the concentration of nanoliposomes (particles/mL), \(t\) is the time (min), and \(k\) is the rate constant (min\(^{-1}\)). Equation 1 can be rearranged and integrated using the following conditions: when \(t = 0\) min, \(C = C_0\), and when \(t = t, C = C_t\), to give Equation 2.

\[
\int_{C_0}^{C_t} \frac{dc}{c} = \int_0^t -kd\text{t}
\]  

(2)

which gives Equation 3:

\[
\ln\left(\frac{C_t}{C_0}\right) = -kt.
\]  

(3)

By taking the exponential and rearranging, we can obtain the final exponential decay Equation 4 as follows:

\[
C_t = C_0e^{-kt}.
\]  

(4)
Additionally, we can obtain the time constant $\tau$ (min) using Equation 5:

$$\tau = \frac{1}{k}.$$  \hspace{1cm} (5)

The values of $\tau$ and $k$ provide key details of the nanoliposome properties and their interactions with the surface of the PDMS microchannel. Owing to their different properties, each nanoliposome has different types of interactions with the PDMS surface. Accordingly, the values of $\tau$ and $k$ can quantitatively describe these interactions. Equation 4 was used to obtain the values of $\tau$ and $k$ by fitting to the adsorption data.

4. Results and discussion

4.1. Quantitative analysis

The data obtained in the form of particles in the ROI [13] were converted to concentration (particles/mL) using the calibration curve shown in Fig. 1. Accordingly, the calibrated data were plotted in Figs. 2, 3, and 4.

Based on the data from Figs. 2, 3, and 4, it was determined that as the particle number in the ROI decreased, the corresponding particle concentration also decreased by approximately 52% to 75%, depending on the type of nanoliposome. This large decrease in particle concentration over time implied that adsorption of the particles likely occurs not only in the ROI, but also in the bulk solution, such that fewer particles are observed in the microchannel.

Next, Equation 4 was rearranged, and the natural logarithm was used to find $k$, where $C_0$ is the concentration at the initial time of 4 min, $C_t$ is the concentration at the final time of 13 min, and $t$ is the difference between the initial and final time which is 9 min. Subsequently, Equation 5 was used to determine $\tau$. The results of these calculations are provided in Table 1.

Table 1. $k$ and $\tau$ calculated for each nanoliposome analyzed.

| Nanoliposome | $k$ (min$^{-1}$) | $\tau$ (min) |
|--------------|----------------|-------------|
| DLPC         | 0.155          | 6.45        |
| DOTMA        | 0.0820         | 12.2        |
| PS           | 0.115          | 8.72        |

DLPC nanoliposomes had the highest $k$ value, which means that it had the fastest adsorption rate, implying that the interaction between DLPC nanoliposomes and the PDMS surface is the
strongest, when compared to the other two types of nanoliposomes. In addition, the $\tau$ value for DLPC nanoliposomes was the lowest, further indicating that it had the fastest adsorption rate and that a larger percentage of nanoliposomes were adsorbed onto the surface, compared to the other nanoliposomes. It is known that DLPC nanoliposomes have hydrophobic interactions with the PDMS surface, while DOTMA and PS nanoliposomes have electrostatic interactions [13]. Therefore, based on the analysis, it was determined that hydrophobic interactions have a stronger effect on the adsorption of nanoliposomes on the surface of PDMS, when compared with electrostatic interactions.

4.2. Other adsorption models

Traditionally, adsorption models such as the linear model, Freundlich isotherm, and Langmuir isotherm are widely used for adsorption analysis [18]. By analyzing the data gathered from repeated adsorption experiments, the equilibrium concentrations from different initial concentrations can be obtained. Accordingly, these models can be used to identify key parameters that help to quantitatively describe the observed adsorption phenomena. However, these adsorption experiments require an adsorption equilibrium state that has to be reached, and accordingly, the observation times are long (one or two hours). Moreover, several experiments need to be carried out so that sufficient data is available to generate an adsorption curve, which increases the overall time and resources required.

Adsorption analysis in the transient phase is possible using the proposed model described in this paper, which allows for quicker analysis and requires less time and resources. By calculating $k$ and $\tau$ values, we obtained parameters that can inform us about the adsorption capabilities of nanoparticles onto a solid surface.

5. Conclusion

With the use of a PDMS microchannel, a platform to analyze the adsorption of NPs on a solid surface was developed. In this study, an adsorption model using the exponential decay equation to find parameters such as the $k$ and $\tau$ values was set up and used to quantitatively analyze the non-equilibrium adsorption of nanoliposomes in a PDMS microchannel. The DLPC nanoliposomes had the highest adsorption rate with a $k$ value of 0.155 min$^{-1}$ and a $\tau$ value of 6.45 min. This implied that the hydrophobic interactions between the DLPC nanoliposomes and the PDMS surface were stronger than the electrostatic interactions between the other nanoliposomes and PDMS surface. The proposed model can be used for quicker adsorption experiments to quantitatively describe the adsorption of nanoparticles onto a solid surface, in comparison with traditional adsorption models, which require a greater time investment.

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highest adsorption rate with a microchannel. The DLPC nanoliposomes had the adsorption of nanoliposomes in a PDMS used to quantitatively analyze the non-equilibrium min\(^{-1}\) and a \(k\) parameters such as the using the exponential decay equation to find was developed. In this study, a n adsorption model the hydrophobic interactions between the DLPC was developed. Moreover, several experiments need to be carried out so that sufficient data is available to generate an analysis, it was determined that hydrophobic interactions with the PDMS surface , compared to the other nanoliposomes and PDMS surface. The surface, compared to the other nanoliposomes and PDMS surface. The adsorption of nanoparticles onto a solid surface, in experiments to quantitatively describe the adsorption of nanoparticles onto a solid surface, in experiments to quantitatively describe the observed adsorption phenomena. However, these adsorption phenomena. However, these adsorption phenomena can be obtained. Accordingly, these models can be used to identify key parameters that help to quantify adsorption experiments, the equilibrium that has to be reached , and accordingly, the possible using the proposed model described in this paper, which allows for quicker analysis and resources required.

\[ \tau = \frac{1}{k} \]

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