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Biomimetic System Characterization: pH-Induced Chromatic Transition and Nanostructural Transformation of Polydiacetyle and Dimyristoylphosphatidylcholine Vesicles Under pH Variation Using Dynamic Light Scattering (DLS) Technique

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Abstract

Blue polydiacetylene (PDA) vesicles were prepared and their response to pH changes was investigated using UV-Vis absorption. The effect of the H^+ and OH^- presence on the size of vesicles was also studied using the dynamic light scattering (DLS) technique. The exposure conditions of pH higher than 9.0 at a temperature of 21 ± 2 °C change the vesicles color from blue to red. Exposure to pH values below 4.0 led to the vesicle's formation of clusters and precipitation. In initial size analysis, the apparent hydrodynamic diameter of the vesicles was 272 nm (pH 5.0). After titration with HCl and NaOH, sizes decrease from 592 nm to 303 nm increasing the pH from 2.0 to 9.0 and it increases again to 324 nm in pH 9.5. This change in the vesicles' size can be explained by the changes in the charges of the carboxyl group present in the polydiacetylene that forms them. Changes in polydiacetylene charges and changes in the content of the vesicles studied due to change in pH explain their instability at pH values below 4.0 and the color change from blue to red, for pH above 9.0.

Keywords

Polydiacetylene, Color transition, Dynamic light scattering, Coulomb interactions

Introduction

Polydiacetylene vesicles (PDA) have been suggested as a tool for the development of sensors and biosensors to be applied in several areas. This interest is due to the fact that PDA-based materials have different colorimetric characteristics, depending on some environmental conditions. Changes in their color, usually from blue to red, in response to some stimuli, such as temperature [1-3], pH [4, 5], mechanical disturbances [6], solvents [7], and recognition of substances [8], have promoted the effective use of PDA vesicles in the development of colorimetric analysis [9-11], chips [12, 13] and biosensors [14, 15]. The correct mechanism to explain color transition from blue to red, due to different stimuli has not been discovered. The most widely accepted is that color transition is associated with a conformational change in polydiacetylene structure. Some authors have suggested mechanisms that attempt to elucidate chromic changes caused by pH variation. Song et al. [16] suggested that color change, from blue to red, provided by pH difference is caused by increased electrostatic repulsion between the head groups due to pH elevation by the addition of NaOH. Kew and

Hall [4] also proposed the same explanation, which may cause disturbances in PDA conformational structure. Boullanger et al. [17] suggested that increased pH leads to ionization of the PDA carboxyl groups, which induces some twists in the polymer structure, thus reducing the energy barrier required for color change. However, a definite mechanism to explain the change of color due to pH variation has not been found yet. Some simple methods can be used to evaluate and characterize the properties of PDA vesicles, including Dynamic Light Scattering (DLS), which is a simple method often used to determine the size of particles in a non-destructive and non-invasive way. Several studies mention the use of this technique for the evaluation and characterization of properties of polymerized PDA vesicles [1, 10, 16-18]. In general, the results of these studies provide important information on the distribution of size and shape of vesicles, organization and morphology of the vesicles, effect of the addition of other components on vesicle formation and effect of molecule detection by vesicles. The use of appropriate methods to characterize color transition of PDA vesicles is important to define some parameters crucial for their application in the construction of colorimetric detection systems. This study assessed the effect of pH on the characteristics of PCDA/DMPC vesicles to explain the transition in their color, from blue to red. Emphasis was placed in the UV visible spectrophotometric detection of color change. DLS technique was used to try to elucidate other changes in the characteristics of PDA vesicles caused by the stimulus studied.

Material and Methods

Preparation of PCDA/DMPC vesicles

The vesicles were prepared by dissolving separately 10.12-pentacosadienoic acid (PCDA), 97% Fluka, and 1,2 - dimyristoyl-sn-glycero-3-phosphatidylcholine (DMPC), Merck 99.8%, in Chloroform, Merck 99.8%, at a concentration of 1 mmol L^{-1} and their mixture, at a ratio of 7:3 (v: v) to a final volume of 10 mL. Chloroform was evaporated using N_2 gas (White Martins) and then, 10 mL of Milli-Q deionized water (18.2 MΩ resistance) was added. The suspension was heated to 60 °C, remained in the sonicator (100 W of potency and 40 kHz of frequency) for 1 hour (Soni-tech sonicador, Ultrasonic cleaning HW 800) and then, the PDA/DMPC solution was filtered through polyvinylidene filer (PVDF 0.45 μm, Millex). The filtrate was cooled at 4 °C for at least 4 hours. The vesicles were polymerized by exposure to 254 nm UV light for 15 mins.

Effect of pH on the stability of vesicles

The vesicle suspension 1 mmol. L^{-1} was titrated potentiometrically with NaOH 0.1 mol L^{-1} solution (pH 9.8). The pH readings were carried out after an incubation period of approximately 5 mins in the potentiometer (DIGMED DM20) and were simultaneously monitored by UV-vis spectrum scanning at wavelength ranging from 700 to 400 nm in a spectrophotometer (GBC UV/vis 918), to evaluate the effect of pH on the possible transition of chromic stage. The HCl 0.1 mol L^{-1} solution (pH 0.98) was also used to assess the chromic response to pH values < 4.0. The analyses were performed at room temperature of 21 ± 2 °C.

Colorimetric response

For color change from blue to red, the colorimetric response (RC) was calculated as a semi-quantitative parameter of the change in chromic properties, according to Equation 1 [19].

$$RC\ (\%) = 100 \times \frac{B_o - B_i}{B_o} \qquad \textit{Equation (1)}$$

Where: $B = A_{blue}/(A_{blue} + A_{red})$; A_{blue} = absorbance at 640 nm and A_{red} = absorbance at 540 nm; B_o and B_i values calculated before and after the change of color, respectively.

Measurements of dynamic light scattering

The size of the vesicles before and after the potentiometric titration with HCl 0.1 mol L^{-1} (pH 0.98) and NaOH 0.1 mol L^{-1} (pH 9.8) was characterized using the dynamic light scattering (DLS) technique. The measurements were performed in Brookhaven Co. equipment, with the use of a TurboCorr correlator, 522 channels and a He-Ne laser (wavelength of 632.8 nm). In DLS measurements, the auto-correlation functions of scattered intensity G(2)(t) = ⟨I(0) I(t) are measured, in which the symbol ⟨...⟩ indicates the ensemble average. These averages were obtained by time average during enough time for statistical fluctuations to become insignificant (typically, 10 mins), since the system can be considered as non-ergodic.

The results were fitted by the standard method of Cumulants, in which the autocorrelation function is adjusted to an exponential with corrections of second order in time [20]:

$$G^{(2)}(t) \cong A + B\ \exp[-2\,\bar{\Gamma}\,t + \gamma t^2] \qquad \textit{Equation (2)}$$

where A and B are fitting parameters; " is the average value of the decay rates of the correlation functions; and γ is the second moment of distribution of decay rates, related to the polydispersity. The diffusion coefficient of the structures, D, is achieved based on the average of the decay rates, given by equation 3.

$$\bar{\Gamma} = Dq^2 \qquad \textit{Equation (3)}$$

where q is the module of the scattering vector given by 4 πn/λ.sen (θ/2), where n is the refractive index of the solvent, λ is the wavelength of the laser and θ is the scattering angle, fixed at 40°. The hydrodynamic diameter, dh, was achieved from the diffusion coefficient by the Stokes-Einstein relation:

$$D = \frac{k_B T}{3\pi\eta d_h} \qquad \textit{Equation (4)}$$

where kB is the Boltzmann Constant; T is the temperature; and η is the viscosity of the solution. Samples were filtered through a 0.45 μm filter before the evaluation and the

measurements were performed at room temperature (25 ± 1) °C. A descriptive analysis of the behavior of the samples was carried out throughout the study.

Results and Discussion

Effect of pH on color transition in PCDA/DMPC vesicles

The chromic behavior of PCDA/DMPC vesicles according to pH was measured for the aqueous suspension of vesicles (initial pH 6.2) using titration with NaOH 0.1 mol L^{-1} and reaching pH values of 7.3; 8.2; 8.9; 9.1; 10.0; 11.0; 12.2 and also with HCl 0.1 mol L^{-1}, reaching pH values of 5.4; 5.0; 3.5; 3.0 and 2.5, in a similar analysis to that used by Kew and Hall [4], for vesicles composed of 10,12 tricosadienoic-acid (TCDA). The spectrophotometric results obtained by the addition of NaOH 0.1 mol L^{-1} and HCl 0.1 mol L^{-1} are shown in figure 1. The PCDA/DMPC vesicles presented an irreversible color transition from blue (maximum absorption of 640 nm) to red (maximum absorption of 540 nm) with pH increased by the addition of NaOH. The red color started to be observed in vesicles at pH above 9.0 and no intermediate chromium phase was observed (Figure 2). On the other hand, the addition of HCl 0.1 mol L^{-1} and the acidification of the vesicles at pH values lower than 4.0 caused no visual change in the colorimetric properties of the vesicles (no change in color) but led to the formation of aggregates of vesicles and consequently increasing the turbidity of the solutions, which prevented the assessment by spectrophotometric measurements.

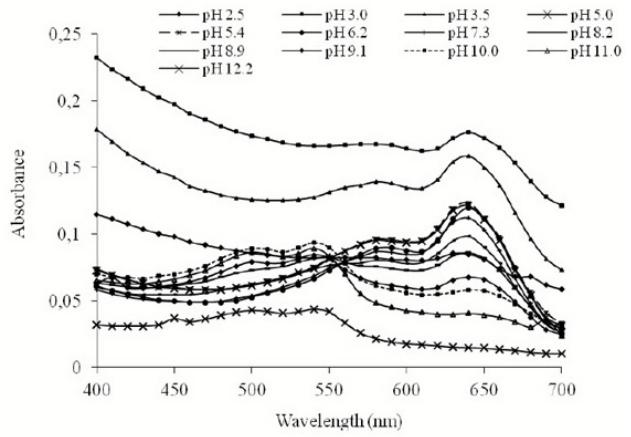

Figure 1: Spectral Curves that represent the absorbance for the suspension of the PCDA/DMPC vesicles after potentiometric titration with HCl 0.1 mol L^{-1} and NaOH 0.1 mol L^{-1}.

The values of the colorimetric response (CR) were 18%, 27% and 40% for pH 9.1; 10.0 and 12.2, respectively (Figure 3). According Oliveira et al. [21], RC of 15% is enough to visualize the color change from blue to red. These results suggest that the conditions of exposure of vesicles to pH values above 9.0 may change the colorimetric properties of the vesicles, while the conditions with pH values lower than 4.0 may promote destabilization of the vesicles.

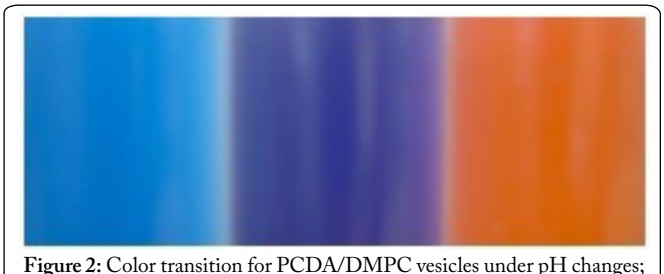

Figure 2: Color transition for PCDA/DMPC vesicles under pH changes; the vesicles shows up (a) a blue color at pH 6.0; (b) a purple color at pH 8.0 and (c) a red color at pH 11.0.

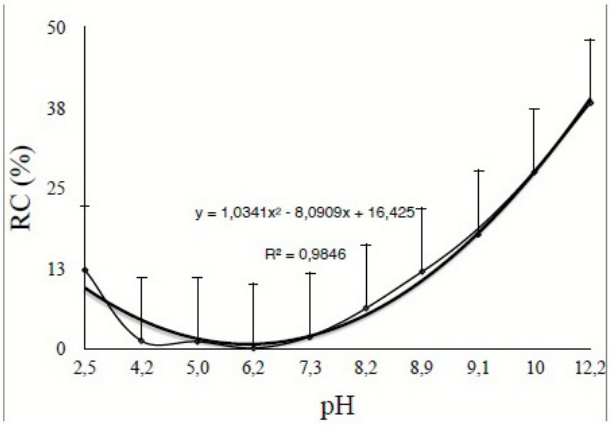

Figure 3: RC curves represent the RC variation for the suspension of the PCDA/DMPC vesicles after potentiometric titration with HCl 0.1 mol L^{-1} and NaOH 0.1 mol L^{-1}.

The results achieved are similar to those presented by Kew and Hall [4] for 10.12 tricosadienoic acid vesicles. These authors observed irreversible change from blue to red with pH increased by the addition of NaOH and the formation of precipitate at pH below 4.0. They also observed the formation of isosbestic point, indicating that color change from red to blue occurred without formation of intermediate color. The same results can be observed in figure 1 for the PCDA/DMPC vesicles. Potisatityuenyong et al. [18] found pH values of 8.3 and RC of approximately 70% for full color transition from blue to red for vesicles consisting only of 10, 12 pentacosadienoic acid; while Cheng et al. [5] found pH values of 6.3; 8.1 and 9.0 for 50% of the maximum color transition from blue to red for vesicles composed of the amino acids glutamic acid, histidine and glutamine, respectively, associated to 10, 12 pentacosadienoic acid. These researchers suggest that the pH required for the transition varies according to the diacetylene that composes the vesicles and also to the presence of other constituents in vesicle structure. Cheng et al. [5] concluded that the pH range for the use of PDA vesicles must be analyzed according to their constitution. These studies reveal that the pH range required to change the color of vesicles depends on the type of PDA and the presence of other compounds in the formation of the vesicles.

Polydiacetylene has been studied as a colorimetric sensing material having self-assembly properties that has two types of color change drawings on the source: 1) the appearance of the color blue and 2) a colorimetric change from blue to pink.

The first color change occurs from the conjugated backbone of alternating double and triple bonds in diacetylene under ultraviolet (UV) irradiation at 254 nm. Radiated PDA vesicles typically show an intensive blue by moving the light absorption band toward the long wavelength because of electronic absorption via the π–π* transition of the electrons in the conjugated backbone. This change of color was generated by increasing the energy gap and enabling the absorption of the light of higher energy by a newly conjugated backbone via the π–π* transition [22, 23]. The mechanism accepted by research community is that the structural transition of PDA's carbonic chain changes from planar to non-planar form, when the compound is exposure to an external stimulus, and this transition can be influence by the lateral chain [24]. Cheng et al. [5] observed that the color transitions of vesicles produced only with tricosadiynoic acid occurred after NaOH addition through the hydrogen bonding of the carboxylic acids of the polymer polar groups. However, Su et al. [10] attributed the reason of the color change by the ionization or deionization of the polar head of polydiacetylene liposomes as result of Coulombic repulsive forces breaking the planar structure of the PDA and forming a new zig-zag polymeric carbonic chain.

Effect of pH on the size of PCDA/DMPC vesicles

It was evaluated the effect of potentiometric titration with NaOH 0.1 mol L^{-1} and HCl 0.1 mol L^{-1} on the size of the PCDA/DMPC vesicles, using DLS. Figure 4 shows the hydrodynamic diameter obtained in these titrations. The initial apparent hydrodynamic diameter of the vesicles was 272 nm (pH 5.0). After the addition of HCl, this value was changed to 314 nm (pH 3.5) and 592 nm (pH 2.0). Both suspensions presented precipitates, indicating that the addition of HCl induced the aggregation of the vesicles, since the H^+ charge deprotone the carboxyl groups of PDA vesicles reducing the electrostatic repulsion. The measured values for the diameter can be related to the structures formed by the association of several isolated vesicles still in suspension, and not to the individual sizes of vesicles. All correlograms were well adjusted by fitting the second order Cumulant model, with an error smaller than 0.5%. Considering that the PCDA polar head is composed of carboxyl groups, and that its dissociation is as indicated in Equation 5, it can be assumed that the addition of HCl shifts the chemical equilibrium in the formation of neutral carboxyl groups (without liquid cargo) so that the Coulomb repulsion becomes less active, due to the presence of negative charges on the surface of the vesicles, thus allowing the formation of aggregates and subsequent precipitation.

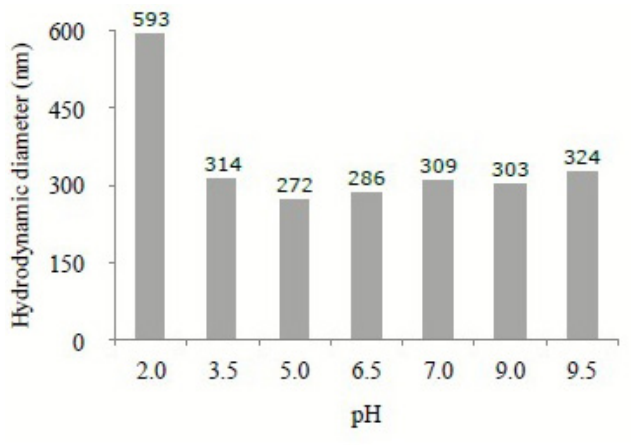

Figure 4: Apparent hydrodynamic diameter (median) according to pH after titration with HCl 0.1 mol L^{-1} and NaOH 0.1 mol L^{-1}.

$$-COOH \leftrightarrow H^+ + -COO^- \qquad Equation\ (5)$$

According to Yoon et al. [25] one of the disadvantages of using PDA in the form of vesicles is the possibility of precipitation of dispersed particles. Considering this fact and the results reported for the spectrophotometric measurements after the addition of HCl 0.1 mol L^{-1}, it was concluded that the use of PCDA/DMPC vesicles as sensors under pH conditions below 5.0 is limited by the possible formation of aggregates and precipitates. On the other hand, titration with NaOH did not lead to such large increase in the size of vesicles and no macroscopic precipitates were observed in the dispersions, indicating that, although a change in its configuration may occur as proposed by some researchers to explain color change [4, 14, 15], the magnitude of this change is not sufficient to cause more significant changes in the size of the vesicles. In this case, there was a displacement in the chemical equilibrium of Equation 2 to form deprotonated carboxyl, which led to greater repulsion of the polar heads of the vesicles and larger distance between them, with consequent increase in the diameter of the vesicles, and the values found were the following: 309 nm for pH 7.0; 303 nm for pH 9.0 and 324 nm for pH 9.5. It is plausible to claim that the values of the hydrodynamic diameter presented refer to the diameters of individual vesicles, not to associations and/or clusters of vesicles. In addition, color change from blue to red was observed at pH higher than or equal to nine. The assessment of this repulsion allows affirming that, for the most extreme repulsions between the carboxyl groups (expected for high pH), there was a change in form that leads to tension along the a polar part of the PCDA, which would change it from the acetylenic form to the butatriene form, thus explaining color change from blue to red.

Conclusion

pH values less than 5.0 leads to aggregation and subsequent precipitation of the vesicles and increased size, while for values higher than 7.0, no aggregate formation was observed, although the effect was an increase in the hydrodynamic diameter of the vesicles. Both effects can be explained by the analysis of the displacement of chemical equilibrium of the carboxyl groups, which affects the Coulomb interactions that stabilize the dispersions.

The DSL technique was adequate to evaluate the changes undergone by polydiacetylene when they changed color from blue to red, which occurred at pH values above nine.

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