Indirect Potentiometric Determination of Polyquaternium Polymer Concentrations
by Equilibrium Binding to 1-Dodecyl Sulfate

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Abstract

Polyquaternium polymers are polycationic polymers that are contained in many hair shampoos and conditioners and are also often added to water to remove organic and inorganic anions by floc formation. While polyquaternium analysis is not trivial, electroanalytical methods have been proposed for their detection using either irreversible emf responses or reversible potential-driven extraction into and out of polymeric sensing membranes. We present here an alternative technique for the determination of a representative polyquaternium polymer, poly(dimethylamine-co-epichlorohydrin) chloride, by equilibrium binding with a singly charged anionic surfactant, 1-dodecyl sulfate. Binding of an anionic surfactant to the polyquaternium polymer simplifies electrochemical detection as the concentration of unbound surfactant can be monitored using the equilibrium Nernstian emf response of ion-exchanger membranes. The latter can be used to determine the nature of the binding interaction and allows for the straightforward determination of polyquaternium polymer concentrations by titration.

Keywords: Polyquaternium polymers, Titration, Ion-Selective Electrodes, Binding Equilibrium, SDS

TOC:
Introduction

Polyquaternium polymers are comprised of repeat units with positively charged ammonium groups. Poly(dimethylamine-co-epichlorohydrin) chloride, which was detected in this work (see Figure 1), is one example. These multiply charged polymers are used for a broad variety of applications, including medical studies, wastewater treatment, consumer products (up to 3 wt %), and environmental contaminant remediation. Due to their widespread use, toxicity studies of these compounds have been pursued. Recent findings suggest that common polyquaternium polymers are toxic to eastern mosquitofish, with EC_{50} values of approximately 1 mg L^{-1}. These EC_{50} values are comparable to that of cetylpyridinium chloride, which is known to be toxic to fish, invertebrates, algae, and rats. Moreover, Monte Carlo simulations of the efficiency a municipal wastewater treatment plants predict a removal rate of polyquaternium polymers commonly contained in cosmetics of less than 25%, which suggests that concentrations attained in the environment could be problematic. However, analytical protocols to measure polyquaternium polymer concentrations in environmental matrices are insufficient, and only limited data is available on the environmental fate and concentrations of these compounds.

Because polyquaternium ions have no distinctive UV-vis or IR absorbing groups and show only broad peaks in NMR spectra, they are surprisingly difficult to detect by spectroscopy. Chromatography of polyquaternium polymers is complicated by the fact that commercial products contain polymeric molecules with a range of molecular weights and, therefore, different charges. To that end, a variety of electrochemical methods have been proposed for the determination of polyquaternium polymer concentrations that can also be used for a wide range of other polyions, that is, polymers with multiple negative or positive charges. These methods overcome multiple difficulties of measuring polyion concentrations electrochemically, which include insensitive Nernstian responses (i.e., responses that are Nernstian but low as a result of the polyionic character of the analyte) and significant differences in interactions with hydrophobic ions and membrane plasticizers, making detection with conventional ion-selective electrodes impossible. Much of this work was directed initially at the quantification of heparin, a lifesaving polyion used to prevent coagulation of blood. Meyerhoff and co-workers developed methods based on the response of ion-selective electrodes to the multiply charged polymer heparin. Their initial method relied on the transfer of the polyanion from aqueous solutions into plasticized poly(vinyl...
chloride) (PVC) membranes doped with hydrophobic cations, which resulted in a nonequilibrium potential response that could be used to determine heparin concentrations. Importantly, this response differed from the typical equilibrium phase-boundary potential for monoanions predicted by the Nernst equation,\textsuperscript{16-18} where a Nernstian response to a polyanion results in a response slope of 59 mV per decade change in concentration divided by the number of charges on each polyanion, a slope too small to experimentally measure for typical polyions. This seminal work was followed by the development of a number of related electrochemical methods for the detection of heparin and other polyions, including polyquaternium polymers.\textsuperscript{12,19-27} Timed applied potentials were used to control extraction of protamine from the sample solutions into a membrane, and subsequent stripping, resulted in potential changes characteristic for the protamine concentration.\textsuperscript{26-27} This approach could also be applied for the indirect detection of heparin by titration with protamine. When the latter is titrated into solutions of heparin, protamine binds to heparin and results in continued potential changes until an excess of protamine is reached. Indicator ions have also been used to signal the endpoint of similar titrations, either with potentiometry or photometry. In this case, the polyion of interest is titrated with a polyion of the opposite charge, resulting in a large decrease in the concentration of the monovalent indicator ions after the endpoint due to binding of those indicator ions to the polyion of opposite charge.\textsuperscript{23-25} In addition, polycation concentrations have been indirectly measured by monitoring the concentration of free polyanions during binding titrations with both non-reversible and reversible techniques.\textsuperscript{19} Automated systems for polyion detection either by non-reversible\textsuperscript{20} or reversible\textsuperscript{21} techniques have also been described.

Here we report on the indirect detection of a representative polyquaternium polymer, poly(dimethylamine-\textit{co}-epichlorohydrin) chloride, using an approach that is arguably less complicated than previously reported electrochemical methods for polyion detection, which we believe offers notable advantages for routine analysis. This technique relies on equilibrium binding between the polyquaternium polymer and a hydrophobic anionic surfactant, such as 1-dodecyl sulfate (DS). The binding interactions are a combination of electrostatic attraction and hydrophobic interactions between the dodecyl chains.\textsuperscript{28} By use of a singly charged anionic surfactant instead of a polyanion to bind the polycation\textsuperscript{19} the concentration of the freely dissolved (not bound) surfactant can be directly monitored through the equilibrium Nernstian response of ionophore-free ion-selective electrodes (ISEs) with plasticized PVC anion-exchange membranes.\textsuperscript{29-30} (For a definition of ionophore-free ion-exchanger
membranes, see ref. 30, p 1595.) This avoids nonequilibrium potential responses to the polyquaternium polymer, simplifying the analysis.

Potentiometric monitoring of the addition of a freely dissolved monovalent anionic surfactant when this surfactant is added to a polyquaternium polymer solution gives a characteristic titration curve that allows the calculation of the polyquaternium polymer concentration in the solution in a straightforward manner. For a quantitative analysis, the strength of interaction between the anionic surfactant and polyquaternium polymer must be known, though. If not known already, this information can be readily obtained for any type of polyquaternium polymer of interest by fitting of the potentiometric titration curve obtained when aliquots of polyquaternium calibrant are added into a solution of the monovalent anionic surfactant.

**Experimental**

**Materials**

All aqueous solutions were prepared using deionized and charcoal-treated water (>18.2 MΩ cm specific resistance) obtained with a Milli-Q PLUS reagent grade water system (Millipore, Bedford, MA, USA). High molecular weight poly(vinyl chloride), 2-nitrophenyl octyl ether, tridodecylmethylammonium chloride, sodium 1-dodecyl sulfate (≥ 99 %, by titration with benzethonium chloride), 1-octyl sulfate, and tetrahydrofuran (anhydrous; inhibitor-free) were purchased from Sigma-Aldrich (St. Louis, MO, USA), poly(dimethylamine-co-epichlorohydrin) (MW = 240,000; repeat unit MW = 137.6) from Accepta (Manchester, UK), and NaCl and Tygon S3 tubing (4.8 mm inner diameter; 7.9 mm outer diameter) from Fisher Scientific (Waltham, MA, USA). All materials were used as received.

**Preparation of Ion-Exchanger Membranes**

Membrane components (200 mg), comprised of 32.5 wt % poly(vinyl chloride), 65.5 wt % 2-nitrophenyl octyl ether, and 2 wt % tridodecylmethylammonium chloride, were dissolved in 1.0 mL of tetrahydrofuran by stirring overnight. The solution was poured into a glass dish (30 mm inner diameter), and the tetrahydrofuran was allowed to evaporate for one day. Discs (1.0 cm) were cut from the resulting master membrane and glued onto Tygon S3 tubing using a plasticized poly(vinyl chloride) glue (66 wt % 2-nitrophenyl octyl ether, and 34 wt % poly(vinyl chloride), dissolved in tetrahydrofuran). The tubing was filled with 1.0 mM NaCl and 0.10 mM sodium...
1-dodecyl sulfate or 1.0 mM NaCl and 0.10 mM sodium 1-octyl sulfate and placed in a solution of the same concentration for at least one day for conditioning. A AgCl-coated Ag wire was placed in contact with the inner solution before measurements.

**Potential Measurements**

Potentials were measured at room temperature in stirred solutions with an EMF 16 potentiometer (Lawson Labs, Malverne, PA, USA) controlled with EMF Suite 1.02 software. All potentials were measured relative to a free-flowing double-junction reference electrode with a 3.0 M KCl bridge electrolyte and AgCl-saturated 3.0 M KCl reference electrolyte (DX200, Mettler Toledo, Switzerland; flow rate into sample \( \approx 1.2 \) µL/h).

**Addition of Poly(dimethylamine-co-epichlorohydrin) to Solutions of Constant Sodium 1-Dodecyl Sulfate Concentration**

After ion-exchanger electrode conditioning, the electrodes were placed in 200 mL of a solution identical to that of the conditioning solution (1.0 mM NaCl and 0.1.0 mM sodium 1-dodecyl sulfate). Then, the sodium 1-dodecyl sulfate concentration was decreased by serial dilution with 1.0 mM NaCl to calibrate the electrode response to 1-dodecyl sulfate. After the lower detection limit was reached, electrodes were again placed in solutions containing 1.0 mM NaCl and 0.1.0 mM sodium 1-dodecyl sulfate. Poly(dimethylamine-co-epichlorohydrin) was added by the addition of small volumes of a stock solution (5.150 g/L) until potentials no longer increased. New electrodes were used after each cycle.

**Addition of Sodium 1-Dodecyl Sulfate to Solutions of Constant Poly(dimethylamine-co-epichlorohydrin) Concentration**

After ion-exchanger electrode conditioning, the electrodes were placed in 200 mL of a solution identical to that of the conditioning solution (1.0 mM NaCl and 0.10 mM sodium 1-dodecyl sulfate). Then, the sodium 1-dodecyl sulfate concentration was decreased by serial dilution with 1.0 mM NaCl to calibrate the electrode response to 1-dodecyl sulfate. After the lower detection limit was reached, electrodes were placed in solutions containing 1.0 mM NaCl and 12.87 mg/L poly(dimethylamine-co-epichlorohydrin). Sodium 1-dodecyl sulfate was added by addition of small volumes of a stock solution (1.0 mM). New electrodes were used after each cycle.
Results and Discussion

Hydrophobic surfactants useful for the indirect detection of polyquaternium polymers as reported in this work must bind to poly(dimethylamine-co-epichlorohydrin) at concentrations that fall within the linear response range of the anion-exchange membranes used for this purpose. To this end, ionophore-free anion-exchanger electrodes were tested for the measurement of 1-dodecysulfate (DS) and 1-octyl sulfate (OS) and provided Nernstian responses to both DS and OS. However, in preliminary experiments addition of poly(dimethylamine-co-epichlorohydrin) to solutions containing OS did not affect the OS concentration. This shows that OS does not bind poly(dimethylamine-co-epichlorohydrin) over the concentration range studied (see Figure S1). Consequently, all further work was performed with DS and not OS.

Ion-Exchanger Electrode Response to Sodium 1-Dodecyl Sulfate

Ionophore-free ion-exchanger electrodes were prepared to respond to the concentration of freely dissolved DS (i.e., not bound to polycationic polymer) within sample solutions. The response of these electrodes to DS in the presence of chloride is given by the Nikolskii-Eisenman equation:

\[ E = E^o + \frac{RT}{zF} \ln (a_{DS} + K_{DS/Cl} a_{Cl}) \]

where \( E \) is the measured potential of the electrochemical cell, \( E^o \) is the standard potential of the cell (including contributions from the reference electrode and the liquid junction to the sample), \( R \) is the ideal gas constant, \( T \) is the temperature, \( z \) is the charge of the measured ion, \( F \) is Faraday’s constant, \( a_{DS} \) is the activity of DS, \( K_{DS/Cl} \) is the selectivity coefficient for DS over Cl\(^-\), and \( a_{Cl} \) is the activity of chloride. All solutions used in this study contained 1.0 mM NaCl to control the ionic strength and activity of chloride. Therefore, eqn 1 can be simplified by assuming the activity coefficient for DS to be a constant that can be combined with \( E^o \) to give the new constant \( E^{''} \):

\[ E = E^{''} + \frac{RT}{zF} \ln ([DS]_{free} + K_{DS/Cl} a_{Cl}) \]

The characteristic response to DS is presented in Figure 2 for three electrodes. The response slope and lower limit of detection were \(-61 \pm 1 \) mV/decade and \(10^{-6.6 \pm 0.1} \) M (95% confidence interval; 6 electrodes), respectively, for calibrations of DS. The thus determined experimental slopes, intercepts \( (E^{''}) \), and the product \( K_{DS/Cl} a_{Cl} \), were used for the fits of all data described in the following sections.
Binding of 1-Dodecyl Sulfate to Poly(dimethylamine-co-epichlorohydrin)

The strength of 1-dodecyl sulfate binding to poly(dimethylamine-co-epichlorohydrin) was determined by monitoring the concentration of freely dissolved DS, \([DS]_{free}\), in a solution of constant total DS concentration upon addition of varying concentrations of poly(dimethylamine-co-epichlorohydrin). Binding of DS to the polymer can be described by the following equilibrium reaction,

\[
[DS]_{free} + [R]_{free} \rightleftharpoons [DS\cdot R] \tag{3}
\]

where \([R]_{free}\) is the concentration of free charged poly(dimethylamine-co-epichlorohydrin) repeat units (where each repeat unit corresponds to one monomer and carries one positive charge; see Figure 1), and \([DS\cdot R]\) represents a repeat unit of the polymer to which a DS molecule has bound. The equilibrium binding constant, \(K\), is then given by:

\[
K = [DS\cdot R] / ([DS]_{free} [R]_{free}) \tag{4}
\]

To relate \(K\) to the experimental data, the binding equilibrium can be combined with experimental observables, as previously reported,\(^3\)\(^4\) resulting in the following eqn:

\[
E = E^\circ + \frac{RT}{zF} \ln \left( K_{DS/Cl} a_{Cl} + \frac{-1 + \sqrt{1 + 4K [DS]_{total} [R]_{total} + 4K [DS]_{total} + (1 - K) [DS]_{total} + K [R]_{total}}}{2K} \right) \tag{5}
\]

where \([DS]_{total}\) is the total concentration of DS, and \([R]_{total}\) is the total concentration of charged polymer repeat units.

Values of \(E\) collected during the addition of poly(dimethylamine-co-epichlorohydrin) to solutions of constant DS concentrations are presented in Figure 3 (for a full set of data see, Figures S2-S8). By adding concentrated aliquots of the polyquaternium polymer, the concentration of free DS is reduced substantially, resulting in large changes in the measured potential, \(E\). Measurements with eight electrodes and fits of the resulting data with eqn 5 were used to characterize the equilibrium constant, \(K\), for DS binding to the individual repeat units of poly(dimethylamine-co-epichlorohydrin), giving \(K = 6.6 \pm 0.6 \times 10^5 \text{ M}^{-1}\) (95% confidence interval). Data near the lower limit of detection for DS (i.e., at higher values of \(E\), where the electrode responds to the chloride background) were excluded from the fits. The thus obtained binding constant was then used to determine the concentration of poly(dimethylamine-co-epichlorohydrin) by titration with DS, as presented in the following section. Note that the lower limit of detection of the ion-exchanger electrode and the binding constant both affect
the lowest concentration of a polyionic polymer that can be measured. In the case of poly(dimethylamine-co-epichlorohydrin), repeat unit concentrations below $10^{-6.6 \pm 0.1}$ M (i.e., $10^{-4.5}$ g/L) cannot be detected because the concentration of DS that binds to the polymer is too small. Poly(dimethylamine-co-epichlorohydrin) would not be measurable even if DS binding were much stronger because then relevant DS concentrations would be below the lower detection limit of the electrode. Note also that increases in the ionic strength of the solution will weaken binding of DS to poly(dimethylamine-co-epichlorohydrin), as similarly shown, e.g., for binding of dodecyltrimethylammonium to poly(styrenesulfonate). Evidently, ionic strength effects could be eliminated by performing the DS additions to polycationic polymer solutions in the presence of a total ionic strength adjuster. For this purpose, phosphate buffer would be ideal because the electrode shows a very high selectivity for DS over phosphate and because phosphate would also control the pH.

Titration of Poly(dimethylamine-co-epichlorohydrin) with Sodium 1-Dodecyl Sulfate

To demonstrate the suitability of the DS-sensitive electrode for the indirect detection of poly(dimethylamine-co-epichlorohydrin), a titration of a solution of this polymer with DS was performed. For this purpose, poly(dimethylamine-co-epichlorohydrin) was added to a solution of 1.0 mM NaCl at a concentration of 12.87 mg/L. To this solution, DS was added until the electrode response to DS approached that of solutions with no poly(dimethylamine-co-epichlorohydrin), indicating that the polycation was saturated with DS (see Figure 4).

The data in Figure 4 was converted to Figure 5 (for full sets of data see Figure S9 and S10), which shows the concentration of bound DS, $[\text{DS}]_{\text{bound}}$, versus the concentration of free DS, $[\text{DS}]_{\text{free}}$. This requires knowledge of $[\text{DS}]_{\text{free}}$, which is calculated from the measured ion-exchanger electrode potential and eqn 2. $[\text{DS}]_{\text{bound}}$ can be obtained from the mass balance for DS (i.e., eqn 5), $[\text{DS}]_{\text{free}}$, and $[\text{DS}]_{\text{total}}$. The latter is known from the amount of DS added during the titration:

$$[\text{DS}]_{\text{total}} = [\text{DS}]_{\text{bound}} + [\text{DS}]_{\text{free}}$$

Figure 5 not only visualizes the effect of DS binding to the polymer but it also allows for straightforward fitting, which allows the determination of the polyquaternium polymer concentration. To do so, the binding constant, $K$, from the previous section is related to the fraction of charged repeat units of the polyquaternium polymer bound to a DS molecule, $\Theta$, using an equation that is formally equivalent to the Langmuir isotherm:
\[ \Theta = 1 - (\text{[R]}_{\text{total}} - \text{[DS]}_{\text{bound}})/\text{[R]}_{\text{total}} = K \text{[DS]}_{\text{free}}/(1 + K \text{[DS]}_{\text{free}}) \] (7)

Solving eqn 7 for \([\text{DS}]_{\text{bound}}\) gives:

\[ [\text{DS}]_{\text{bound}} = [\text{R}]_{\text{total}} K \text{[DS]}_{\text{free}}/(1 + K \text{[DS]}_{\text{free}}) \] (8)

The data of Figure 5 can be fitted with Eqn 8 with \([\text{R}]_{\text{total}}\) as the fitting variable because both \([\text{DS}]_{\text{free}}\) and \(K\) are known. The former is known from the ion-exchanger electrode response, and \(K\) is characteristic for the DS and the polycationic polymer of interest and can be determined as described in the previous section.

Three titrations of a solution that contained poly(dimethylamine-co-epichlorohydrin) chloride were performed (for a full set see Figures S11 and S12). The concentration of poly(dimethylamine-co-epichlorohydrin) obtained from this fit was 12.8 ± 1.2 mg/L (95 % confidence interval), which is within error the same as the known concentration of the polymer of 12.87 mg/L.

**Conclusions**

Binding of 1-dodecyl sulfate to poly(dimethylamine-co-epichlorohydrin) was characterized by monitoring the concentration of freely dissolved surfactant with ionophore-free ion-exchanger electrodes. Experimental data are consistent with a 1:1 binding stoichiometry between the surfactant and the individual charged repeat units of the polymer and were fitted to give a binding constant of \(K = 6.6 \pm 0.6 \times 10^5 \text{ M}^{-1}\) (95% confidence interval). Using this equilibrium constant, titration curves collected during the addition of 1-dodecyl sulfate to solutions containing poly(dimethylamine-co-epichlorohydrin) chloride were fitted with a single variable, i.e., the concentration of polyquaternium charged repeat units. This technique simplifies the determination of polycation concentrations as it (i) does not entail a second type of polymer, (ii) relies on an equilibrium rather than a non-equilibrium response of the electrode to the monovalent surfactant, and (iii) does not require regeneration of the electrode prior to subsequent measurements. It is important to note that binding of the monovalent surfactant to the polycation could be affected by the presence of other ionic surfactants that are part of many cosmetic and consumer products that contain polyquaternium polymers.\(^{36}\) However, removal of these components and replacement with more hydrophilic salts is readily achievable through the use of ion-exchange membranes.\(^{19}\) The approach described here could also be extended to the measurement of other polyions. In particular, binding studies of DS to the polycation
protamine and of cationic surfactants to the polyanion heparin, both of which are on the World Health Organization’s list of essential medicines, is currently being pursued in our laboratory.

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Supporting Information

Supporting information includes figures that show the response of ion-exchanger electrodes to 1-octyl sulfate, measured potentials during the addition of poly(dimethylamine-co-epichlorohydrin) to 1.0 mM DS solutions, measured potentials during the addition of DS to a 12.87 mg /L poly(dimethylamine-co-epichlorohydrin) solution, and concentrations of bound and free DS in a poly(dimethylamine-co-epichlorohydrin) containing solution. This material is available free of charge on the Web at http://www.jsac.or.jp/analsci/

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References


**Figure Captions**

**Figure 1.** Repeat unit structure of poly(dimethylamine-co-epichlorohydrin) chloride.

**Figure 2.** Response of ion-exchanger electrodes to DS. Black squares, red circles, and blue triangles represent individual electrode responses.

**Figure 3.** Measured potentials during the addition of poly(dimethylamine-co-epichlorohydrin) (black squares) to a 1.0 mM DS solution (1.0 mM NaCl background). The blue line represents a fit of the experimental data based on eqn 5.

**Figure 4.** Blue filled squares: Measured potentials during the addition of DS to a 12.87 mg/L poly(dimethylamine-co-epichlorohydrin) solution (1.0 mM NaCl background). Black empty squares: Measured potentials during the dilution of DS (1.0 mM NaCl background). The blue line represents the concentration of bound DS, [DS]_{bound}, and the black line to corresponding concentration of free DS, [DS]_{free}.

**Figure 5.** Concentrations of bound and free DS in a poly(dimethylamine-co-epichlorohydrin) containing solution. Concentrations were calculated from using eqn 2 and the data in Figure 4. Blue line represents a fit to eqn 7 with [R]_{total} = 18.6 µM.
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