Published in final edited form as:

Anal Methods. 2016 August 7; 8(29): 5806–5811. doi:10.1039/C6AY01748G.

Detecting Levels of Polyquaternium-10 (PQ-10) via Potentiometric Titration with Dextran Sulphate and Monitoring the Equivalence Point with a Polymeric Membrane-Based Polyion Sensor

Stephen A. Ferguson^a, Xuewei Wang^a, and Mark E. Meyerhoff^{a,†}

^aDepartment of Chemistry, University of Michigan, Ann Arbor, MI 48109-1055, USA

Abstract

Polymeric quaternary ammonium salts (polyquaterniums) have found increasing use in industrial and cosmetic applications in recent years. More specifically, polyquaternium-10 (PQ-10) is routinely used in cosmetic applications as a conditioner in personal care product formulations. Herein, we demonstrate the use of potentiometric polyion-sensitive polymeric membrane-based electrodes to quantify PQ-10 levels. Mixtures containing both PQ-10 and sodium lauryl sulfate (SLS) are used as model samples to illustrate this new method. SLS is often present in cosmetic samples that contain PQ-10 (e.g., shampoos, etc.) and this surfactant species interferes with the polyion sensor detection chemistry. However, it is shown here that SLS can be readily separated from the PQ-10/SLS mixture by use of an anion-exchange resin and that the PQ-10 can then be titrated with dextran sulphate (DS). This titration is monitored by potentiometric polyanion sensors to provide equivalence points that are directly proportional to PQ-10 concentrations.

Graphical abstract

Introduction

Polymeric quaternary ammonium salts (polyquaterniums) represent a class of polyions that have found increasing use in industrial and cosmetic applications around the world (e.g., industrial flocculation agents and as conditioners in personal care products).^{1–3} These

[†]Corresponding author: mmeyerho@umich.edu.

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here].
See DOI: 10.1039/x0xx00000x

compounds are known to be toxic to certain aquatic species.⁴ Further, manufacturers need to add appropriate amounts of these species to personal care product formulations to elicit the desired effects (e.g., thickening agents for hair, etc.).

It is often found that polyquaterniums (PQs) of low charge density are used in personal care products (e.g., shampoos).⁵ More specifically, the quaternized hydroxyethylcellulose compound, PQ-10 (see Figure 1a), is commonly present within shampoo formulations containing anionic surfactants.^{6,7} In these formulations PQ-10 is solubilized with relatively high concentrations of anionic surfactants (e.g., sodium lauryl sulfate (SLS)).⁶ After dilution, which normally takes place during the bathing process, the anionic surfactant:PQ-10 ratio reaches a level at which an anionic-polycationic complex precipitates. This facilitates the desired hair-conditioning effect to take place, allowing hair to lie flat. For this reason PQ-10, and other PQs, are also known as antistatic agents.^{5,6} As such, it has become increasingly important to quantitate these compounds using analytical techniques.

Since PQ-10 is a polycationic species, the application of electrochemical polyion-sensitive polymeric membrane ion-selective electrodes (ISEs), introduced in the early 1990s,^{8–10} for the detection and quantification of this compound in various shampoo formulations should prove useful. However, anionic surfactants have been known to give large potentiometric responses with poly(vinyl chloride) (PVC)-based ISEs.^{11,12} Since these surfactants are customarily found in shampoo formulations this poses an analytical challenge in the application of the polyion sensor technology to the quantification of PQ-10 in such samples. Therefore, to provide a reliable and reproducible detection method for the measurement of PQ-10 in such samples with polyion-sensitive ISEs, it will be necessary to remove SLS from solutions containing both polycationic PQ-10 and anionic surfactant in a way that does not alter the level of PQ-10 present. Herein, we describe the application of a simple ion-exchange treatment method, initially introduced by Weber and Kuter¹³ for the separation of SLS from solutions containing protein and urea, to effectively remove SLS from solutions containing both PQ-10 and SLS. The resulting solution is then titrated with dextran sulphate (DS) (see Figure 1b) and monitored using a single-use polyanion-sensitive polymeric membrane ISE as the detector to provide equivalence points directly proportional to PQ-10 levels.

Experimental

Reagents and materials

DS sodium salt from *Leuconostoc* (MW 500,000), glacial acetic acid, and double junction reference electrode inner and outer filling solutions were purchased from Fisher Scientific (Waltham, MA). SLS (97.98%) was obtained from Calbiochem (Billerica, MA) and tridodecylmethylammonium chloride (TDMAC) was purchased from Polysciences (Warrington, PA). Bis(2-ethylhexyl) sebacate (DOS), high molecular weight PVC, tetrahydrofuran (THF), Dowex[®] monosphere anion-exchange resin (hydroxide form) (584 μm particle size), and sodium hydroxide pellets were products of Sigma-Aldrich (St. Louis, MO).

Membrane Preparation and EMF Measurements

All experiments were performed at ambient temperature (22°C). Polymeric membranes were cast using the method described by Craggs et al.¹⁴ Each membrane was batch fabricated using membrane cocktails containing 800 mg of ingredients dissolved in 8 mL of THF. Each batch of membrane cocktail contained 66% PVC, 32.5% DOS, and 1.5% TDMAC (w/w) dissolved in 8 mL of solvent. All ingredients were dissolved in anhydrous THF and allowed to mix overnight. Once cocktails were completely solubilized in THF, each batch was poured into a glass casting ring (8.75 cm i.d.) placed on a homemade glass slide (14 × 14 cm) and allowed to evaporate at room temperature overnight. After the solvent was evaporated, small discs (5 mm i.d.) were cut using a cork borer and integrated into Ostec electrode bodies (Oesch Sensor Technology, Sargans, Switzerland). The inner filling solution consisted of a 10 mM NaCl electrolyte. Potentiometric responses were measured against an external Ag/AgCl double junction reference electrode. Potential values were recorded by averaging the last 10 equilibrium EMF values three minutes after each DS injection. The solutions being titrated were stirred via stir bar for the duration of the titration.

Ion-exchange of SLS in PQ-10/SLS Mixtures and Subsequent Manual or Automated Potentiometric Titration of PQ-10 with DS

All mixtures of PQ-10/SLS as well as the DS titrant were dissolved in a background electrolyte of 10 mM NaCl. Five solutions of 5% (w/v) SLS were dissolved in 10 mM NaCl. Known amounts of PQ-10 were also added to four of the five SLS solutions (0.1, 0.2, 0.3, and 0.4% (w/v), respectively). These solutions were allowed to dissolve completely before being diluted to mark. Each solution was subsequently diluted 1:50 with 10 mM NaCl to provide a working solution for extraction and measuring the PQ-10 response.

Dowex resin was exhaustively washed prior to use in the conventional manner described by Weber and Kuter.¹³ If resin was not used immediately in an ion-exchange process, the beads were stored in distilled water. Approximately 120 mL of anion-exchange resin was packed into an appropriately sized glass column. Working solutions were prepared via 1:50 dilutions using 10 mM NaCl as a diluent and allowed to flow through the column. Four fractions of each mixture were collected. After the fractions were collected, 50 mL aliquots of each ion-exchange treated sample were used for titrations. Alternatively, thick suspensions were used for ion-exchange in the conventional manner described by Craggs et al.¹⁴ Suspensions were allowed to mix on a rotator for no less than 30 minutes for complete ion-exchange prior to sample titration. Each aliquot was acidified prior to titration via addition of 50 µL of glacial acetic acid. The working and reference electrodes were allowed to obtain a stable baseline EMF prior to the start of the titration. For manual titrations, the 50 mL aliquots were subsequently titrated with DS in 10 mM NaCl and the titration was followed using single-use polyanion-sensitive polymeric membrane ISEs as described previously for titrations of polycationic protamine with polyanionic heparin.⁹ For automated titrations, 50 mL aliquots of increasing concentrations of PQ-10 in 10 mM NaCl were titrated with DS in 10 mM NaCl using a dual-syringe infusion/withdrawal pump (Cole-Parmer, Vernon Hills, Illinois); there was no surfactant present in these samples initially, therefore, ion-exchange was not necessary. Regeneration of the column resin was achieved by exhaustively flushing the beads with a 0.1 M NaOH solution prior to the next resin treatment.

Results and Discussion

SLS Removal via Ion-Exchange

As SLS is a strong interfering species when using polyanion-sensitive polymeric membrane ISEs, it is necessary to remove SLS from the sample prior to detection. Figure 2 illustrates the effective removal of SLS from an aqueous solution containing both SLS and PQ-10. A 100-fold dilution of a mixture of 0.5% (w/v) PQ-10 and 5% (w/v) SLS solution was prepared using 10 mM NaCl as a diluent in both the stock and diluted samples. The diluted sample was then subjected to ion-exchange using a suspension of anion-exchange resin as described by Weber and Kuter.¹³ After the ion-exchange process the resin was allowed to settle to the bottom of the container and a 5 mL aliquot of the supernatant was added to a 5 mL solution of 10 mM NaCl background electrolyte into which a single-use polyion sensor had previously obtained a stable baseline EMF value; this resulted in a total 200-fold dilution of the stock 0.5%/5% PQ-10/SLS mixture. This process was also completed using a 100-fold dilution of the stock 0.5%/5% PQ-10/SLS solution which did not undergo an ion-exchange process. As shown in Figure 1, the EMF responses of the working electrode toward the diluted sample that was not subjected to ion-exchange resulted in a large negative EMF response due to the presence of SLS within the sample. In contrast, the diluted sample that was treated with the ion-exchanger resulted in the EMF remaining at the baseline value established in the 10 mM NaCl background electrolyte. This indicates that the SLS concentration was reduced to a level at which there is negligible interference to the TDMAC-based polyanion sensor membrane.

Verification of Non-Adsorption of PQ-10 to Ion-Exchange Resin

Prior to quantification of the remaining PQ-10 in solution it is necessary to ensure that PQ-10 does not interact with the anion-exchange resin after a sample is treated. Figure 3 depicts how PQ-10 is not adsorbed to the anion-exchange resin. This figure shows two potentiometric titrations of identical solutions of 25 µg/mL PQ-10 in 10 mM NaCl. One aliquot of this solution was not subjected to the anion-exchange resin while the other aliquot was subjected to the resin followed by addition of glacial acetic acid to acidify the sample; a 50 mL aliquot of sample subjected to anion-exchange resin was treated with 50 µL of glacial acetic acid. Each of the resulting solutions were titrated with DS until an endpoint was obtained and first derivative plots were employed to determine the equivalence point for each titration. The equivalence points generated by these two titrations resulted in only a 4.3% difference. These data suggest that there is no significant adsorption of PQ-10 to the anion-exchange resin during the ion-exchange process. However, it should be noted that the total EMF generated from the acidified ion-exchanged sample showed a marked increase at the endpoint when compared to the sample that was not subjected to anion-exchange resin. This suggests that the addition of a weak acid such as acetic acid can increase the total EMF of this potentiometric titration of PQ-10 with DS, indicating that at lower pH values, the polyanion sensing membrane exhibits more significant response to the DS polyanionic species. This is in agreement with findings reported by Schwake et al.¹⁵ in which potentials for DOS plasticized PVC membranes doped with various quaternary ammonium species were reported for different sodium salts, including sodium acetate.

Quantification of PQ-10 via Potentiometric Titration

An appropriate method was needed to effectively detect the remaining PQ-10 in solution after SLS removal. As there are two specific methods (indirect and direct detection) that can be used for this task, it was necessary to determine which would provide appropriate and reliable data for PQ-10 quantification. Because PQ-10 is known to have a charge of approximately +1 per disaccharide unit resulting from the quaternary ammonium group attached to the hydroxyethyl side-chain^{16,17} it can be expected that PQ-10 would yield a relatively small total EMF (compared to the more characterized responses of polyionic species heparin and protamine) if direct detection with a polycation sensing membrane electrode based on dinonylnaphthalene sulfonate (DNNS) were to be employed.¹⁸ Hence, in this work, the titration of PQ-10 with the high charge density DS species and use of the polyanion sensor described above was pursued. Figure 4a illustrates typical titrations of varying levels of PQ-10 using DS as the titrant as monitored by the TDMAC-based polyanion sensing membrane electrode after SLS removal. It is demonstrated that as more PQ-10 is present in the original sample (with SLS also initially present), after removing the SLS, the equivalence points of the titration curves obtained are directly proportional to the concentration of PQ-10 in the samples. This indicates that even with the low charge density of the PQ-10 species, a very strong ion-pair formation between DS and PQ-10 occurs within the aqueous phase. Figure 4b illustrates the calibration curve obtained when plotting the equivalence points of the titrations in terms of amount of DS required (using first derivative plots to obtain equivalence point values) vs. PQ-10 in the sample, illustrating the expected linear relationship. Using this method, PQ-10 levels as low as 20 µg/mL can be detected.

Figure 5 shows the effect of the hydroxide ion levels on the polyanion-sensitive polymeric membrane. Solutions of 10 mM NaCl were prepared with known amounts of NaOH. This resulted in 10 mM Cl⁻ solutions at four different pH values. As illustrated in the plot, each polyanion response shows a decreased negative slope as the response deviated further from the super-Nernstian response reported by Ma et al.⁹ These data suggest that the pH of the extracted solution will need to be closely monitored after the anion-exchange process. If the pH of the solution is too high, the pH can be adjusted using an appropriate acid which contains an anion that would not interfere significantly with the polyanion sensing membrane. The initial potential of the electrode is controlled by the Cl⁻ level in the NaCl electrolyte solution.^{19,20} In addition, as notated in Table 1, it was determined that the starting potentials of each titration decreased as pH increased. This demonstrates that excess hydroxide begins to effect the sensor prior to the addition of polyanionic DS. To circumvent this issue, one might try to use a suitable buffer. While phosphate buffered saline (PBS) is an ideal buffer for biological applications, the use of an anion-exchange resin (hydroxide form) causes the released hydroxide concentration to exceed the buffer capacity of conventional concentrations of PBS. For samples containing variable amounts of SLS the amount of anion-exchange resin will need to be adjusted accordingly. This will result in variable pH values and increase the potential of exceeding the buffer's capacity to maintain a constant pH value. Hence, adjustment of the pH of the final PQ-10 sample to a relatively fixed, low pH value after the anion-exchange process to remove SLS will help ensure that the total EMF changes observed for the titrations remain relatively similar.

Automated Titrations of PQ-10 via Syringe Pump-Based Potentiometric Detection Method

To increase the sample throughput of the titration method of PQ-10, it would be advantageous to use a syringe pump that would facilitate continuous titrant injection into the sample in addition to reducing random error related to injection placement and/or timing (i.e., injections were made every three minutes for the manual titrations described above). Figure 6a illustrates initial results from efforts targeted at this approach. Syringe pump titrations were performed using samples with increasing concentrations of PQ-10 in 10 mM NaCl; no surfactant was initially present in these samples and anion-exchange was therefore not performed. Here, each increasing concentration of PQ-10 is shifted further to the right. This resulted in the expected equivalence points as higher concentrations of DS are added and results are in excellent agreement with the manual PQ-10 titrations performed above. Figure b illustrates the calibration data of the resulting equivalence points calculated via first derivative plots from each titration curve. In addition, the total EMF for these samples was markedly lower than the acidified effluents collected after treatment with anion-exchange resin. This further illustrates how the addition of a weak acid such as acetic acid can increase the total EMF for a given polyanion when these electrochemical polyanion-sensitive polymeric membrane ISEs are used.

Conclusions

Over the last 20+ years, potentiometric polyion sensing has grown to be a useful analytical method to detect and quantify different polyions in various chemical environments.^{9,18,21} More recently, potentiometric polyion sensing has also been further developed through its application to potentiometric aptasensing,^{22,23} biomedical analyses without the use of moving components,²⁴ and the reversible potentiometric detection of biomedically relevant polyions.^{25–28} At the same time, PQ-10 has found increasing use in cosmetic applications such as shampoo formulations for its ability to act as a conditioner to aid in repairing damaged hair. As PQ-10 is a polycationic species that forms strong complexes with polyanions, as shown here, the use of a polyanion-sensitive electrode for its quantification via an indirect titration method is a promising new approach that can be applied in various quality control applications in industrial settings. Also, the addition of the ion-exchange method described here is shown to be effective in the reduction of any potential SLS interference. This enables the reliable detection of PQ-10 via the potentiometric titration of PQ-10 using DS as a titrant polyanion.

Acknowledgments

This work was supported by the Microfluidics in Biomedical Sciences Training Program at the University of Michigan (NIH grant number T32 EB005582) and Procter and Gamble.

Notes and references

1. Gruber, J.V. Principles of polymer science and technology in cosmetics and personal care. Gruber, J.V.; Goddard, E.D., editors. New York: Marcel Dekker Inc.; 1999. p. 217-274. E.D. Goddard
2. Zocchi, G. Hand of cosmetic science and technology. Barel, A.O.; Paye, M.; Maibach, H.I., editors. New York: Informa Healthcare USA Inc.; 2009. p. 357-370. Barel, M
3. Cumming J, Hawker D, Chapman H, Nugent K. Water, Air, Soil Pollut. 2011; 216:441–450.

4. Biesinger KE, Stokes GN. J Water Pollut. Control Fed. 1986; 58:207–213.
5. Cumming JL, Hawker DW, Matthews C, Chapman HF, Nugent K. Toxicol. Environ. Chem. 2010; 92:1595–1608.
6. Rodriguez R, Alvarez-Lorenzo C, Concheiro A. Eur J Pharm Biopharm. 2003; 56:133–142. [PubMed: 12837491]
7. Miyake M, Kakizawa Y. Colloid Polym. Sci. 2002; 280:18–23.
8. Ma S, Yang V, Meyerhoff M. Anal. Chem. 1992; 64:694–697. [PubMed: 1580363]
9. Ma SC, Yang VC, Fu B, Meyerhoff ME. Anal. Chem. 1993; 65:2078–2084. [PubMed: 8372971]
10. Yang ME, Ma Victor C, Liu Shu-Ching, Brown Dong, Meyerhoff Richard B. ASAIO J. 1993; 39:M195–M201. [PubMed: 8268527]
11. Alizadeh N, Mahmodian M. Electroanalysis. 2000; 12:509–512.
12. Gerlache M, Sentiirk Z, Vir JC, Kauffmann JM. Anal. Chim. Acta. 1997; 2670:59–65.
13. Weber K, Kuter DJ. J Biol. Chem. 1971; 246:4504–4509. [PubMed: 5106387]
14. Craggs A, Moody G, Thomas J. J Chem. Educ. 1974; 51:541–544.
15. Schwake A, Cammann K, Smirnova AL, Levitchev SS. 1999; 393
16. Rodriguez R, Alvarez-Lorenzo C, Concheiro A. J Control. Release. 2003; 86:253–265. [PubMed: 12526822]
17. Klemm PDD, Schmauder PDT, Heinze HansPeter Prof. Dr. Biopolym. Vol. 6 Polysaccharides II Polysaccharides from Eukaryotes. 2002:275–287.
18. Buchanan SA, Kennedy TP, MacArthur RB, Meyerhoff ME. Anal. Biochem. 2005; 346:241–245. [PubMed: 16213460]
19. Zubrowska M, Wróblewski W, Wojciechowski K. Electrochim. Acta. 2011; 56:6114–6122.
20. Tan SSS, Hauser PC, Wang K, Fluri K, Seiler K, Rusterholz B, Suter G, Krüttli M, Spichiger UE, Simon W. Anal. Chim. Acta. 1991; 255:35–44.
21. Yun VC, Meyerhoff Jong Hoon, Yang Mark E. Anal. Biochem. 1995; 224:212–220. [PubMed: 7710074]
22. Ding J, Gu Y, Li F, Zhang H, Qin W. Anal. Chem. 2015; 87:6465–6469. [PubMed: 26044085]
23. Ding J, Chen Y, Wang X, Qin W. Anal. Chem. 2012; 84:2055–2061. [PubMed: 22263631]
24. Wang X, Wang Q, Qin W. Biosens. Bioelectron. 2012; 38:145–150. [PubMed: 22672765]
25. Gemene KL, Meyerhoff ME. Anal. Chem. 2010; 82:1612–1615. [PubMed: 20121058]
26. Lester J, Chandler T, Gemene KL. Anal. Chem. 2015; 87:11537–11543. [PubMed: 26485655]
27. Shvarev A, Bakker E. J Am. Chem. Soc. 2003; 125:11192–11193. [PubMed: 16220929]
28. Shvarev A, Bakker E. Anal. Chem. 2005; 77:5221–5228. [PubMed: 16097762]

Novelty

This manuscript reports a novel and facile method for PQ-10/SLS separation and subsequent PQ-10 quantification via potentiometric titration.

Fig. 1.

(a) Chemical structure of PQ-10. (b) Chemical structure of dextran sulphate.

Fig. 2. EMF response of a single-use polyanion sensor to 5 mL of a 1:100 dilution of extracted vs. non-extracted samples of a 0.5%/5% PQ-10/SLS solution after dilution.

Fig. 3. Non-adsorption verification of PQ-10 onto the anion-exchange resin. One solution was subjected to anion-exchange/acidification and one was unperturbed. Equivalence points for both aliquots are quite similar.

Fig. 4.

(a) Titration curves of PQ-10 at various concentrations with DS as titrant in 10 mM NaCl background electrolyte. The data points for each curve represent the average EMF from three electrodes placed in the same PQ-10 solution. (b) Calibration curve from the data under (a).

Fig. 5. Hydroxide ion interference to TDMAC-doped polyion-sensitive polymeric membrane ISE at various pH values. Each curve is a single titration monitored by three electrodes simultaneously placed in the same solution.

Fig. 6.

(a) Syringe pump-assisted titration of increasing concentrations of PQ-10 with DS as titrant. A flow rate of 200 $\mu\text{L}/\text{min}$ of a 0.5 mg/mL titrant solution of DS was used for sample volumes of 50 mL. The data points for each curve represent the average EMF from three electrodes placed in the same PQ-10 solution. (b) Calibration curve from the data under (a). The standard deviations of the 20, 40, 60, and 80 $\mu\text{g/mL}$ PQ-10 samples are 2.19, 1.85, 2.10, and 4.49, respectively.

Table 1

Starting potentials of various solutions of 25 µg/mL PQ-10 dissolved in 10 mM NaCl at different pH values. These starting potentials are averages of three electrodes placed in the same electrolyte solution.

pH	Average Equivalence Point ([DS] (µg/mL))	Starting potential (mV)
8.43	13.05	142.16
8.79	15.66	132.38
9.85	10.45	101.10
10.71	NA	-14.96