Potentiometric determination of zinc in supplement tablets using a Ca-ion selective electrode

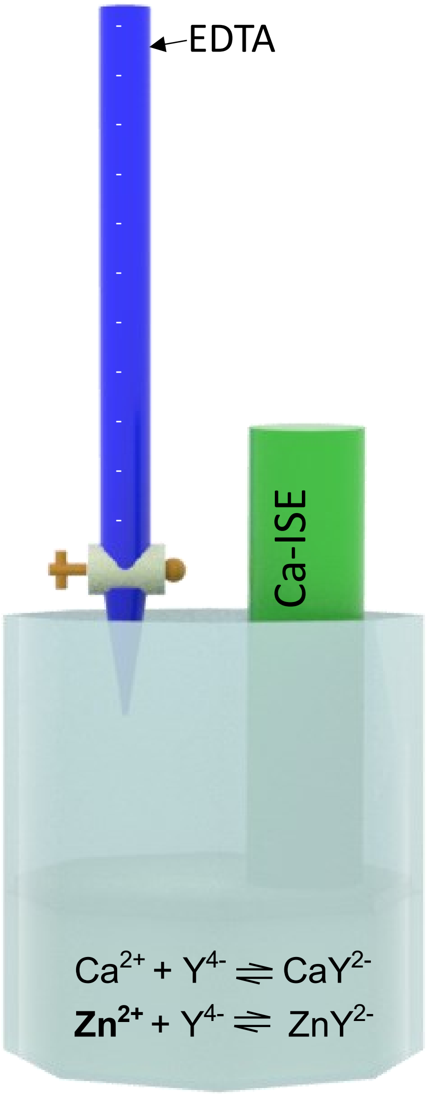
Hugo Y. Samayoa-Oviedo, Emily Halpern, Samantha A. Mehnert, and Julia Laskin*

Department of Chemistry, Purdue University, West Lafayette, IN 47907, United States

*Corresponding author:

Julia Laskin, Tel: 765-494-5464, Email: jlaskin@purdue.edu

TOC



ABSTRACT

The laboratory experiment presented here describes the use of a calcium ion-selective electrode (Ca-ISE) to determine the concentration of zinc in a supplement tablet. This approach was developed to show students how to expand the range of applications of Ca-ISE to enable the determination of metal ions other than Ca^{2+}. To determine the concentration of Zn^{2+}, students dissolved the sample in a Ca-EDTA buffer solution and used EDTA as titrant. We discuss with students the importance of a fixed pH and ionic strength for the accurate analytical quantification. Students also use colorimetric titration of the same sample with murexide as an indicator to determine the concentration of Zn^{2+}. They used statistical tools to confirm that the two approaches provide similar results. Students concluded that both titrations overestimate the amount of zinc in a tablet by 3-5% in comparison with the known value reported by the manufacturer and discussed factors that affect the accuracy of Zn^{2+} determination.

Keywords

Upper-Division Undergraduate, Analytical Chemistry, Communication/Writing, Hands-On Learning/Manipulatives, Acids/Bases, Aqueous Solution Chemistry, Ion Selective Electrodes, Titration/Volumetric Analysis.

INTRODUCTION

Complexometric titration with EDTA is amongst the most widely-used analytical techniques in undergraduate laboratory experiments[1–5] and is commonly conducted using either colorimetric or potentiometric methods. Potentiometric titrations are powerful approaches since they enable accurate quantification of analytes[6–8] and the determination of thermodynamic constants.[9–11] In a typical potentiometric titration, an indicator electrode measures the change of potential with the addition of the titrant to the solution. This requires that the indicator electrode has a stable response to the activity of the analyte in solution. Membrane ion-selective electrodes (ISE) fulfill this requirement as they contain an ionophore membrane that selectively binds the ion of interest. In the membrane, a majority of analyte ions are bound to ionophores and a small fraction is present as free ions. When the electrode is immersed in a solution with the analyte, a potential difference is created due to the diffusion of a small fraction of the analyte from or to the ionophore (depending on the activity gradient across the interface). The potential difference created in this process is measured against the potential of a reference electrode, usually Ag/AgCl, placed inside the ISE. In order to determine the activity of a different ion than the one the ISE is selective to, the potential reading of the ISE must respond to changes in the concentration of the free titrant ligand in solution. To ensure this, the following conditions must be met: 1) the solution must contain a stable metal ion buffer formed by the ion the ISE is selective to and the ligand to be used in the titration, 2) the metal ion to be determined in the titration should form a less stable complex that the one present in the metal ion buffer and, 3) only one titratable metal ion can be appreciably present in addition to the metal ion in the buffer.[12] For example, a Ca-ISE may be used to measure the activity of zinc ion by performing an EDTA titration using a low-concentration Ca-EDTA metal ion buffer. Initially, additions of EDTA to the solution result in the formation of metal ion-EDTA complexes during which the reading of the Ca-ISE remains constant. However, after the equivalence point, there is an excess amount of EDTA in solution which shifts the position of the Ca-EDTA equilibrium thus, altering the potential difference across the ISE. This experiment in an undergraduate chemistry laboratory provides an opportunity for students to combine different concepts related to classical complexometric titrations and broadens their understanding of the experimental design by showing them an unconventional way of using an ISE.

Zinc determination in complex mixtures has been widely explored in undergraduate laboratory experiments using gravimetric[13] and gasometric[14] analysis, atomic absorption spectroscopy,[15] complexometric[1,2] and precipitation[16] titrations. From a biological point of view, zinc plays a vital role in the immune function of organisms[17] and its deficiency is associated to 4% of global child morbidity and mortality.[18] Zinc supplements are available commercially and, when properly used, maintain sufficient zinc levels in the body. In the most common over-the-counter zinc supplement tablets, zinc is present as zinc gluconate. However, the presence of insoluble minor components in zinc supplement tablets such as sugars and vegetarian coatings may complicate zinc determination using volumetric analysis. The quantification of zinc in supplement tablets offers an excellent opportunity to assert the importance of an accurate measurement in a complex matrix. Herein, we present an experimental procedure for the determination of zinc content in zinc supplement tablets using a potentiometric titration with Ca-ISE and EDTA as a ligand. Students used statistical tests to compare the potentiometric titration with a colorimetric titration to verify that both techniques yield similar results. Furthermore, students successfully identified that the quantification using the Ca-ISE relies on fixing the ionic strength and pH of the solution to optimal values that ensure an accurate reading of the ISE and eliminates interferences caused by side acid/base equilibria of the reactants, respectively.

EXPERIMENT DETAILS

Pre-lab requirements. Prior to attending the lab, students are provided with the lab protocol and narrated Powerpoint presentation in which a teaching assistant gives an overview of the lab. Once the students read and listened to the narrated presentation, they take a pre-lab quiz. In the pre-lab quiz, students are asked five questions aimed to test their understanding of the experimental procedure. These activities ensure that students are familiar with the experiment before coming to the lab. A summary of the experimental procedure is provided here, and further details can be found in the SI.

Principle of the measurement. To perform this experiment, a metal ion-buffer of calcium ion and EDTA (Y^{4-}) must be present in solution. The metal ion-buffer is formed by mixing equimolar solutions of calcium ion and EDTA at pH=10 so that the following equilibrium is established.[19]

$$Ca^{2+} + Y^{4-} \rightleftharpoons CaY^{2-} \quad K_f = \frac{[CaY^{2-}]}{[Ca^{2+}][Y^{4-}]} = 10^{10.69} \qquad (1)$$

Ca^{2+} forms hydroxides at high pH. The effect of this side equilibrium on the formation constant of CaY^{2-} is accounted for using the conditional formation constant ($K_f{}'_{pH=10}$), which includes the fraction of free calcium ions (α_{Ca}) and fully deprotonated EDTA ions ($\alpha_{Y^{4-}}$,) present in solution at a given pH. (At pH=10, $\alpha_{Ca} = 0.996$ and $\alpha_{Y^{4-}} = 0.360$):

$$K_f{}'_{pH=10} = K_f \alpha_{Ca}\, \alpha_{Y^{4-}} = 10^{10.69} \times 0.996 \times 0.36 = 10^{10.24} \qquad (2)$$

The Ca-ISE responds to the activity of calcium ions according to the following equation:

$$E = k + \beta \frac{0.059}{2} log A_{Ca^{2+}} \qquad (3)$$

where k and β are the electrode constants, E is the measured potential [V], and A_{Ca} is the activity of free calcium ions [M]. At a constant ionic strength, the activity coefficient is constant, and equation (3) can be re-written in terms of the concentration of calcium ions:

$$E = k' + \beta \frac{0.059}{2} log[Ca^{2+}] \qquad (4)$$

where k' is a modified constant k that includes the activity coefficient.

In the presence of the Ca-EDTA buffer in solution, $[Ca^{2+}]$ in equation (4) can be expressed in terms of the Ca-EDTA conditional formation constant (K_f'). Combining equations (1), (2), and (4), we obtain equation (5):

$$E = k' + \beta \frac{0.059}{2} log \frac{[CaY^{2-}]}{K_{f'}[Y^{4-}]} \qquad (5)$$

Equation (5) may be rearranged using the properties of logarithms to give equation (6):

$$E = k' + \beta \frac{0.059}{2} log \frac{[CaY^{2-}]}{K_{f'}} - \beta \frac{0.059}{2} log[Y^{4-}] \qquad (6)$$

The titration is designed in such a way that both K_f' and $[CaY^{2-}]$ in equation (6) remain constant. K_f' is kept constant by maintaining constant ionic strength and pH. Furthermore, to minimize changes in $[CaY^{2-}]$ due to dilution, we make sure that the volume of the titrated solution is much greater than the added volume of the titrant. Finally, through rearrangement of equation (6), we obtain:

$$E = S - \beta \frac{0.059}{2} log[Y^{4-}] \qquad (7)$$

Equation 7 indicates that, at constant pH, the ISE responds to changes in EDTA concentration in the analyzed solution. Increasing the concentration of EDTA will decrease the voltage measured by the electrode. Equation (7) may be used to simulate the Zn^{2+} titration curve obtained at a constant pH using Ca-ISE in a solution containing a Ca-EDTA metal ion buffer. For this equation to be accurate, the conditional formation constant of ZnY^{2-} should be smaller than the conditional formation constant of CaY^{2-}. Otherwise, EDTA will preferentially bind to the free Zn^{2+} ions which will displace Ca^{2+} ions from CaY^{2-} complexes and alter the Ca-ISE reading.

In the experiment presented herein, zinc is titrated by reaction with EDTA ($K_f = 10^{16.50}$ and $K_f'{}_{pH=10}$ $10^{8.54}$) at pH=10 using the Ca-EDTA buffer described earlier. Under these conditions, the CaY^{2-} complex is more stable than the ZnY^{2-} complex, which is critical to the accurate determination. At pH 10, most of the Zn^{2+} is present as insoluble $Zn(OH)_2$ (pK_s=15.52). However, the high conditional formation constant of ZnY^{2-} at pH 10 of $10^{8.54}$ is a strong driving force for the substitution of hydroxyl groups with EDTA to form a soluble ZnY^{2-} complex. Indeed, the extent of Zn^{2+} reaction with EDTA forming ZnY^{2-} complex of 99.94% is high enough for this reaction to be considered quantitative. Nevertheless, the kinetics of this reaction are relatively slow, and constant mixing and stabilization between measurements is necessary to ensure that it goes to completion.

The titration is performed as follows using the solutions prepared as described in the SI section: a solution of EDTA at a fixed pH and ionic strength is placed in a burette. The analyte is dissolved in a solution that contains the Ca-EDTA metal ion buffer with the same pH and ionic strength as the titrant and placed in a beaker. A Ca-ISE electrode is immersed in the beaker. At the beginning of the titration, the potential on the ISE is established by the equilibrium in equation 1. The addition of a small amount of EDTA to the solution results in the formation of the ZnY^{2-} complex, which consumes free EDTA quantitatively. The measured potential changes only slightly in this step. At the equivalence point, there is no Zn^{2+} left to titrate and the remaining free EDTA in solution will decrease the potential as described in equation 7 by binding some of the free Ca^{2+} ions in the ionophore membrane. In other words, the equilibrium in equation 1 is always present in solution. At the equivalence point, any increase in $[Y^{4-}]$ will cause reaction (1) to shift towards products. The corresponding decrease in $[Ca^{2+}]$ results in a voltage drop measured by the ISE as described in equation 4.

Participants. In total, 108 students participated in the laboratory experiment. 134 students were originally enrolled in this class and were either3rd or 4th year students. Table 1 shows the distribution of majors of the students enrolled in the class. The students were organized into sections of 21 with seven stations available to perform the experiments with most students working in groups of three.

Table 1. Majors of the students enrolled in the class.

Major	**Number of students**	**Major**	**Number of students**
Chemistry	78	Occupational Health Science	3
Environmental Health Sciences	13	Biochemistry (Biology)	2
Chemical Engineering	6	Biomedical Engineering	2
Environmental Geoscience	5	Electrical Engineering	2
Biochemistry Honors	3	Pharmaceutical Sciences	2
Biology	3	Other	12

Health Science PreProfessional	3

Lab experiment. The experiment was conducted during a lab period of 3 hours. Students work in groups of three to perform both the potentiometric and colorimetric titration of Zn^{2+}. To compare the results from the potentiometric and the colorimetric titration, each group performs each titration in triplicate. All the solutions are prepared in an ammonia/ammonium chloride buffer (pH = 10 and 0.2 M ionic strength). Keeping the pH constant during the titration is important as both Zn and EDTA can undergo acid/base side reactions that affect the outcome of the experiment. Since the ISE responds to activities and not concentrations, by fixing the ionic strength we eliminate errors in the measurement due to changes in activity coefficients, which otherwise may occur during the titration.

Each group of students is provided with three commercial Zn supplement tablets (CVS Health Zinc 50 mg tablets). First, they weigh all three tablets to determine the average mass of the tablets. Next, the students pulverize and homogenize the tablets using a mortar and pestle. For the colorimetric titration, the students suspend the powder in ~50 mL of the ammonia/ammonium chloride buffer solution described previously and add 3-4 drops of murexide indicator (In^{2-}) to the resulting solution. For the potentiometric titration, the students use a different ammonia/ammonium chloride buffer solution that contains a Ca-EDTA buffer (2×10^{-4} M CaY^{2-}, prepared from the $CaCl_2$ dihydrate and EDTA disodium salt dihydrate salts as described in the SI) provided to them at the beginning of the lab. In both titrations, 0.01 M EDTA prepared in the ammonium buffer solution is used as a titrant. Because Zn supplement tablets contain compounds that are not soluble in the buffer solution, the sample that is prepared for analysis is not a homogenous solution. As described in the previous section, $Zn(OH)_2$ is formed at pH 10. As a result, the analyte solution must be continuously stirred to allow EDTA to extract Zn from $Zn(OH)_2$ through ligand exchange to form ZnY^{2-}.

For the colorimetric titration, the equivalence point is determined by the color change of the solution from yellow to red/pink as shown in Figure 1. The initial color of the solution is yellow due to the presence of $ZnIn_{(aq)}$ complex. After the equivalence point, EDTA chelates Zn^{2+} thus releasing In^{2-} to the solution, which results in a reddish-pink color.

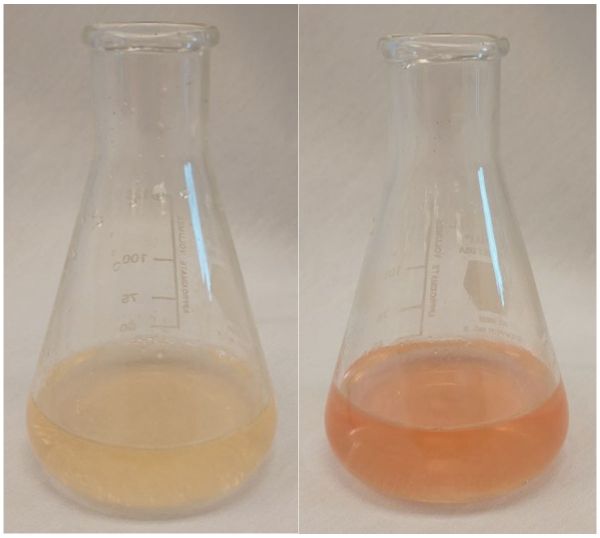


Figure 1. Solution with the analyte for the colorimetric titration before (left) and after (right) the equivalence point.

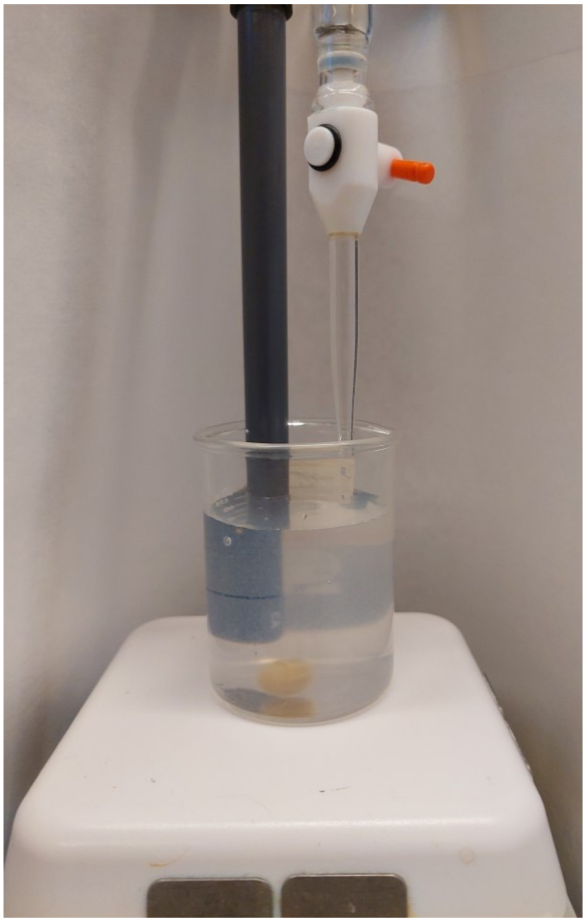


Figure 2. Experimental set-up for the potentiometric titration. The solution is continuously stirred using a stir bar. Ca-ISE electrode is immersed in the solution up to the minimum level mark.

The experimental setup for the potentiometric titration is shown in Figure 2. The sample is placed in a 100 mL beaker and continuously stirred using a magnetic stir bar to improve the reaction rate. The Ca-ISE is immersed into the solution and a burette containing EDTA is positioned above the beaker. In this study, we used a Ca-ISE from Vernier (Beaverton, OR) connected to an iPad, and the potential was measured using the Vernier Graphical Analysis program.

HAZARDS

Students are required to wear appropriate lab clothing including splash goggles and gloves during the entire lab session. The pH 10 ammonia/ammonium chloride buffer solution is corrosive.

RESULTS AND DISCUSSION

In total, 108 tablets were analyzed across all the lab sections. The distribution of the weights of the tablets is shown in Figure 3. According to the manufacturer, each tablet has 50 mg of Zn^{2+}. Considering the average weight of a tablet of 0.58 g, the expected zinc content per tablet is 8.6% m/m.

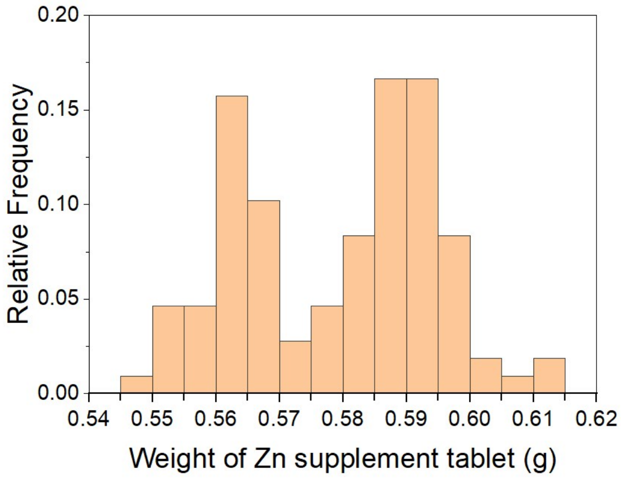


Figure 3. The experimental distribution of the weights of Zn supplement tablets (n = 108, $\bar{x}$ = 0.58 g, s = 0.02 g).

For the colorimetric titration, the volume at the equivalence point was determined based on the color change of the solution from yellow to red/pink as shown in Figure 1. A typical potentiometric titration plot is shown in Figure 4. The volume at the equivalence point is determined from the inflection point of the sigmoidal plot. The accurate value at the inflection point is obtained by examining the second derivative of the titration curve. The students compute the second derivative of the measured potential to obtain the second derivative plot shown as a red trace in Figure 4. Subsequently, they calculate the volume at the equivalence point by finding the x-intercept of an imaginary line drawn between the adjacent maximum and minim points of the second derivative plot as exemplified in Figure 4. The analytical expression used to find the volume at the equivalence point is shown in equation (8).

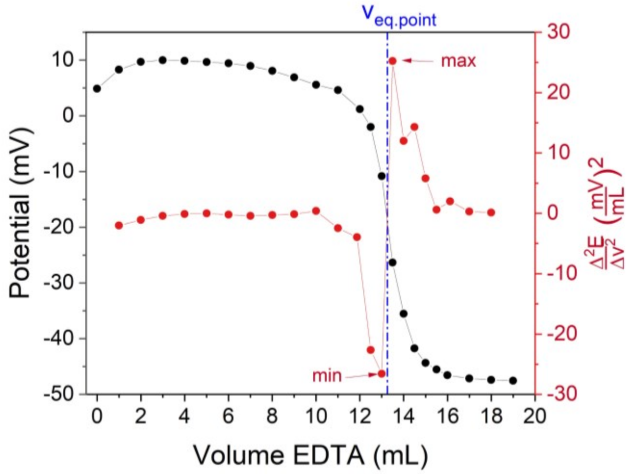


Figure 4. The experimental potentiometric titration curve obtained using a Ca-ISE (black) and the second derivate of the titration curve used to find the equivalence point of the potentiometric titration (red) as described in the text. The equivalence point is indicated with the blue dashed line and marked as $v_{eq.point}$. The maximum and minimum points of the second derivative plot used to determine the equivalence point are also marked in the figure.

$$v_{eq.point} = \frac{x_{min}\times\frac{y_{max}-y_{min}}{x_{max}-x_{min}} - y_{min}}{\frac{y_{max}-y_{min}}{x_{max}-x_{min}}} = x_{min} - \frac{y_{min}}{\frac{y_{max}-y_{min}}{x_{max}-x_{min}}} \qquad (8)$$

Where (x_{min}, y_{min}) and (x_{max}, y_{max}) are the minimum and maximum points of the second derivative, respectively, labeled in Figure 4.

The zinc content per tablet is calculated using equation 9:

$$\%Zn\left(\frac{g}{g}\right) = v_{eq.point} \times C_{EDTA}\frac{M_{Zn}}{m_{sample}} \times 100 \qquad (9)$$

Where $v_{eq.point}$ is the volume at the equivalence point [L], C_{EDTA} is the concentration of EDTA [M], M_{Zn} is the molar mass of elemental zinc [g/mol] and, m_{sample} is the experimental weight of the sample used in titration [g].

The results from the entire class for the determination of Zn % content in supplement tablets, obtained from both titrations resemble a normal distribution as shown in Figure 5. When compared against the true value of 8.6% specified by the manufacturer, both the colorimetric and potentiometric methods overestimated the amount of Zn by 4.7% and 3.5%, respectively. The error in the titration determinations could be due to the presence of insoluble $Zn(OH)_2$ in the sample used for analysis. Although the complexation with EDTA is highly favorable at this pH, an excess amount of EDTA above the equivalence point may be required to drive the reaction to completion. These observations provide the basis for discussion of the strengths and limitations of the technique used for analysis with students. For example, this sample could be pre-treated to remove the interferences or analyzed with a technique that is not sensitive to the presence of insoluble $Zn(OH)_2$, such as X-ray fluorescence or atomic flame spectroscopy. Furthermore, it is also possible that the amount of zinc in the tablet reported by the manufacturer is lower than the real amount on the sample given that these tablets are not pre-approved by FDA before public release.[20] A t-test comparison between the result obtained with each titration and the known value indicates that both values are different at a 95% significance level ($t_{calc,colorimetric} = 7.18$, $t_{calc,ISE} = 5.39$, $t_{table} = 2.05$).

Students also performed an F-test to compare the variances of both methods. Based in the results reported by the students, we conclude that the variances are not significantly different ($F_{critical} = 1.35 < F_{95\%,\ d.o.f.1,2=30} = 1.84$). The comparison t-test assuming equal variances indicates that there is no significant difference (at the 95% confidence level) between both titrations ($t_{calc} = 0.141 < t_{95\%,\ d.o.f=62} = 2.00$). These results agree with the distributions shown in Figure 5 and support the argument that using a Ca-ISE as a sensor for the determination of zinc in commercial zinc supplement tablets yields a result that is comparable to the one obtained by a classical colorimetric titration.

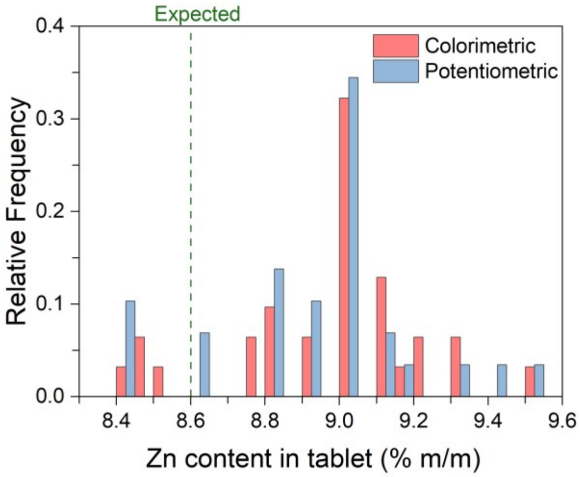


Figure 5. Histograms of the Zn content in Zn supplement tablets determined by colorimetric titration (red bars, n = 31, $\bar{x} = 9.0\%$, s = 0.3 %) and potentiometric titration (blue bars, n = 29, $\bar{x} = 8.9\%$, s = 0.3%). The dashed green line shows the expected value of 8.6%.

EVALUATION OF LEARNING OBJECTIVES

Students had one week to prepare a full lab report in which they evaluated their results using statistical analysis and discussed the effect of side equilibria (protonation of EDTA and precipitation of zinc) on the accuracy of the complexometric titration. The rubric used to evaluate the lab reports is provided in the SI. The quantitative section of the lab was evaluated by assessing the student's response to the following three questions:

1. What is the percent content of zinc in commercial zinc supplemental tablets determined by colorimetric and potentiometric titrations?
2. Are the results obtained from both methods significantly different from that reported by the manufacturer?
3. Are the results obtained by both methods significantly different from each other?

All the answers were supported by the appropriate F- and t-tests. Most of the students found that there was no significant difference between both titration methods. For each group of students, the results of the comparison varied based on the repeatability of their measurements. 87% of the students found that the Zn content determined by the colorimetric titration was not significantly different from the expected value. For the potentiometric titration, 79% of the students found that the result was similar to the expected value. In comparison, close to 100% of the students reported that both titration methods yielded similar results.

Students were provided with fractional composition diagrams of EDTA and Zn as a function of pH (included in the SI). Using these diagrams, students were asked to indicate which species are present in the buffer solution at pH 10 and provide a chemical explanation of why the titration can be performed at pH 10 despite the presence of side reactions in solution. The conceptual section of the lab was evaluated by students' responses to the following questions:

1. Explain the role of the buffer in the Zn-EDTA titration.
2. Identify the Zn and EDTA chemical species present in solution at pH 10.
3. Explain why the titration can be performed at pH 10.
4. Explain how a metal ion buffer can be used for a complexometric titration, in which the ion-selective electrode is not selective towards the analyte.
5. Explain why it is important to keep the ionic strength constant during the potentiometric titration.

CONCLUSIONS

In summary, we introduced a new methodology to perform a potentiometric titration of zinc in commercial supplement tablets using EDTA as a titrant and Ca-ISE as a detector. Compared with a colorimetric titration using murexide as an indicator, both titrations yielded similar results, but they overestimate the amount of Zn by 3-5% compared with the value specified by the manufacturer. This error may be related to the formation of insoluble $Zn(OH)_2$ in solution, which requires an excess of EDTA to drive the reaction to completion. This experiment also allows students to think about the effect of pH on side equilibria occurring in solution during the titration (precipitation of Zn as $Zn(OH)_2$ at high pH and, protonation of EDTA at low pH) and the importance of using pH buffer for accurate determination of zinc. It also encourages students to conceptualize the role of the ionic strength and the presence of a Ca-EDTA metal ion buffer in the experimental design. Due to the high stability of the CaY^{2-} complex, Zn^{2+} can be accurately determined in the analyte solution by titration with EDTA. Future implementations of this activity will benefit from including the measurement of Zn solutions of known concentration to validate the performance of the technique. Finally, this experiment presents an opportunity for students to use statistical tools (such as F- and t-tests) to evaluate the performance of two different methods and facilitate the comparison of the experimental results with the value specified by the manufacturer.

ACKNOWLEDGEMENTS

The authors thank Paul Bower for his support in preparing the solutions needed for the experiment, as well as the Chemistry Department at Purdue University for funding. We also thank Miranda Weigand, Manxi Yang and Michael Espenship for their feedback while running the labs. JL acknowledges partial support from the National Science Foundation (NSF- 2108729).

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

SUPPORTING INFORMATION

The Supporting Information is available on the ACS Publications website at DOI: 10.1021/acs.jchemed.XXXXXXX. [ACS will fill this URL in.]

SI1. Prep-lab notes, pre-lab quiz questions, lab protocol for students, rubric to evaluate lab report, fractional abundance diagrams of EDTA and Zn as a function of pH.

SI2. Overview of the experiment for students prior to the lab.

REFERENCES

(1) G. Novick, S. Complexometric Titration of Zinc: An Analytical Chemistry Laboratory Experiment. *J. Chem. Educ.* **1997**, *74* (12). https://doi.org/10.1021/ed074p1463.

(2) Borges Simões, G.; Victor e Silva Badolato, P.; Dante Ignácio, M.; Coelho Cerqueira, E.

Determination of Zinc Oxide in Pharmaceutical Preparations by EDTA Titration: A Practical Class for a Quantitative Analysis Course. *J. Chem. Educ.* **2020**, *97* (2), 522–527. https://doi.org/10.1021/acs.jchemed.9b00939.

(3) Yang, S.-P.; Tsai, R.-Y. Complexometric Titration of Aluminum and Magnesium Ions in Commercial Antacids. An Experiment for General and Analytical Chemistry Laboratories. *J. Chem. Educ.* **2006**, *83* (6). https://doi.org/10.1021/ed083p906.

(4) L. Garvey, S.; Shahmohammadi, G.; R. McLain, D.; L. Dietz, M. Determination of Calcium in Dietary Supplements: Statistical Comparison of Methods in the Analytical Laboratory. *J. Chem. Educ.* **2014**, *92* (1), 167–169. https://doi.org/10.1021/ed400543p.

(5) Belle-Oudry, D. Quantitative Analysis of Sulfate in Water by Indirect EDTA Titration. *J. Chem. Educ.* **2008**, *85* (9). https://doi.org/10.1021/ed085p1269.

(6) T. Lieu, V.; E. Kalbus, G. Potentiometric Titration of Acidic and Basic Compounds in Household Cleaners. *J. Chem. Educ.* **1988**, *65* (2). https://doi.org/10.1021/ed065p184.

(7) A. Volmer, D.; Curbani, L.; A. Parker, T.; Garcia, J.; D. Schultz, L.; Marcel Borges, E. Determination of Titratable Acidity in Wine Using Potentiometric, Conductometric, and Photometric Methods. *J. Chem. Educ.* **2017**, *94* (9), 1296–1302. https://doi.org/10.1021/acs.jchemed.6b00891.

(8) Stoodley, R.; R. Rodriguez Nuñez, J.; Bartz, T. Field and In-Lab Determination of Ca2+ in Seawater. *J. Chem. Educ.* **2014**, *91* (11), 1954–1957. https://doi.org/10.1021/ed4005722.

(9) E. Grabowski, L.; R. Goode, S. Determining a Solubility Product Constant by Potentiometric Titration To Increase Students' Conceptual Understanding of Potentiometry and Titrations. *J. Chem. Educ.* **2017**, *94* (5), 636–639. https://doi.org/10.1021/acs.jchemed.6b00460.

(10) E. Goldberg, D. Formation Constants of a Metal-Amine System: Potentiometric Titration Experiment. *J. Chem. Educ.* **1962**, *39* (7). https://doi.org/10.1021/ed039p328.

(11) Berger, M. Potentiometric Determination of Chloride in Natural Waters: An Extended Analysis. *J. Chem. Educ.* **2012**, *89* (6), 812–813. https://doi.org/10.1021/ed2005449.

(12) J. Blaedel, W.; H. Laessig, R. Continuous EDTA Titrations with a Dropping Mercury Electrode. Automated Titrations Based on Nonsymmetrical Curves. *Anal. Chem.* **2002**, *37* (10), 1255–1260. https://doi.org/10.1021/ac60229a022.

(13) W. Burgstahler, A. Gravimetric-Gasometric Determination of Zinc on Galvanized Nails. *J. Chem. Educ.* **1992**, *69* (7). https://doi.org/10.1021/ed069p575.

(14) Yang, S.-P. How Many Atomic Layers of Zinc Are in a Galvanized Iron Coating? *J. Chem. Educ.* **2007**, *84* (11). https://doi.org/10.1021/ed084p1792.

(15) K. Pomeroy, R.; Drikitis, N.; Koga, Y. The Determination of Zinc in Hair Using Atomic Absorption Spectroscopy. *J. Chem. Educ.* **1975**, *52* (8). https://doi.org/10.1021/ed052p544.

(16) Fabre, P.-L.; Reynes, O. Determination of Copper and Zinc in Brass: Two Basic Methods. *J. Chem. Educ.* **2010**, *87* (8), 836–837. https://doi.org/10.1021/ed100259b.

(17) Kambe, T.; Tsuji, T.; Hashimoto, A.; Itsumura, N. The Physiological, Biochemical, and Molecular Roles of Zinc Transporters in Zinc Homeostasis and Metabolism. *Physiol. Rev.* **2015**, *95* (3), 749–784. https://doi.org/10.1152/physrev.00035.2014.

(18) Penny, M. E. Zinc Supplementation in Public Health. *Ann. Nutr. Metab.* **2013**, *62(suppl 1* (Suppl.

1), 31–42. https://doi.org/10.1159/000348263.

(19) Smith, R. M.; Martell, A. E.; Motekaitis, R. J.; Smith, R.; Motekaitis, R. J. NIST Critically Selected Stability Constants of Metal Complexes Database; 2004.

(20) Andrews, K. W.; Roseland, J. M.; Gusev, P. A.; Palachuvattil, J.; Dang, P. T.; Savarala, S.; Han, F.; Pehrsson, P. R.; Douglass, L. W.; Dwyer, J. T.; Betz, J. M.; Saldanha, L. G.; Bailey, R. L. Analytical Ingredient Content and Variability of Adult Multivitamin/Mineral Products: National Estimates for the Dietary Supplement Ingredient Database1,2. *Am. J. Clin. Nutr.* **2016**, *105* (2), 526–539. https://doi.org/10.3945/ajcn.116.134544.