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Ion-chromatographic quantitation of fluoride and acetate Statistical comparison of calibration curves from two similar eluents

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Abstract

Using a Dionex AS14 column and tightly controlled concentration ranges [center point±10 relative % (where the term 'relative %' refers to the quantity 'true minus predicted', divided by the true and multiplied by 100)], various calibration curves for hydrofluoric acid and acetic acid are generated and examined statistically. The curves are constructed for two Na_2CO_3–$NaHCO_3$ mobile phases: (1) 2.5 m*M* Na_2CO_3–3.4 m*M* $NaHCO_3$, and (2) 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$. With the former eluent, the two peaks are retained out of the void volume, but do not show baseline separation. Nearly complete resolution can be achieved with the weaker solution. However, peak shapes suffer and retention times lengthen. The overall goal is not to provide a completely validated method; rather, the aim is to provide the necessary statistical data for evaluating a calibration curve's acceptability. A Dionex DX 500 ion chromatograph and JMP statistical software were utilized for the study. © 1998 Elsevier Science B.V.

Keywords: Calibration curves; Statistical analysis; Fluoride; Acetate; Inorganic anions

1. Introduction

In the semiconductor industry, researchers frequently need to quantify hydrofluoric acid and/or acetic acid, sometimes with high accuracy. Anion-exchange chromatography is a logical choice for such assays. Historically, though, quantitation of fluoride and acetate has been a challenge, especially under isocratic conditions, where these two usually elute in the water dip.

Several chromatographers have addressed this topic [1–14], but none investigated a recently introduced column, the Dionex AS14. This product affords a promising possibility for this determination. The usual mobile phase is 3.5 m*M* sodium carbonate–1.0 m*M* sodium bicarbonate. In test chromatograms, fluoride and acetate are in a ratio of 1:4; both are retained out of the void volume, although complete baseline separation is not achieved [15]. (A borate buffer is an alternative eluent suggested by the vendor. However, isocratic conditions do not separate this pair completely, either. Gradient chromatography does a better job, but in many laboratories, such a procedure is undesirable for routine use. Since carbonate-bicarbonate mobile phases are the ones of choice in the author's laboratory, this buffer pair was employed here.)

This paper describes an AS14 calibration study for quantifying hydrofluoric acid and acetic acid. Two different sets of eluent conditions are examined: a carbonate–bicarbonate mixture in the vendor-suggested concentration ranges, and a much weaker solution that affords nearly baseline separation. Tradeoffs among retention times, peak shapes and

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calibration-curve data are discussed, giving the researcher well defined choices for the analysis.

In all work, the separations were performed on a Dionex DX 500 ion chromatograph and statistical analyses were carried out using JMP software.

2. Experimental

2.1. Materials

For preparation of eluents and standards, deionized water (18 mΩ cm) was provided by a point-of-use water-purification system (Ahlfinger Water, Dallas, TX, USA). Sodium carbonate and sodium bicarbonate from Fluka (Ronkonkoma, NY, USA) were used to prepare individual eluent solutions of 20 m*M* each, as well as a mixed solution that was 0.1 m*M* in each constituent. The mobile phases were kept under pressure with helium throughout their life. For preparing calibration standards, the following acids were obtained from VWR Scientific (West Chester, PA, USA): Baker Analyzed 48–51% reagent HF and Baker Analyzed 100% reagent CH_3CO_2H; actual assay values were 49.1 and 100.0%, respectively.

Standards were prepared by mass in 4-oz polypropylene specimen containers from Fisher Scientific (Pittsburgh, PA, USA). Acids and diluents were transferred by pouring, with delivery of the final mass via polyethylene transfer pipets from Fisher.

2.2. Apparatus and columns

A Dionex (Sunnyvale, CA, USA) DX 500 ion chromatograph was utilized for all work. Unless otherwise noted, all instrument modules and consumables were from Dionex. Analytical columns used were an IonPac AG14 Guard (50 mm x 4 mm) with AS14 Analytical (250 mm×4 mm). To deliver the eluent mix of 2.5 m*M* Na_2CO_3–3.4 m*M* $NaHCO_3$, a GP40 gradient pump mixed the constituents (20 m*M* Na_2CO_3, 20 m*M* $NaHCO_3$ and deionized water) in the ratio of 12.5:17:70.5. This same pump was used to provide the pre-mixed 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$. For all work, the flow-rate was 1.5 ml/min. Post-column eluent suppression was accomplished with an Anion Self-Regenerating Suppressor (ASRS-I, 4 mm) in the recycle mode; detection was via a CD20 conductivity detector at an output range of 10 μS. A 10 μl sample loop was employed.

Instrument control and data collection were performed with a personal computer and Dionex PeakNet software. Statistical analyses and calculations were carried out using JMP software (SAS Institute, Cary, NC, USA). For all calibration curves, a straight-line model was proposed for the data. Ordinary least squares was used as the fitting technique.

2.3. Preparation of standards

In order to matrix-match any samples subsequently applied to a calibration curve, acids were used to prepare standards. Separate stock standards (7.75%, w/w, HF and 27.7%, w/w, acetic acid) were prepared from the commercial concentrated acids; the resulting solutions were used throughout the study. Every day, an intermediate standard (2 g of the stock to 100 g with water) was made for each acid. These daily solutions were used to prepare the mixed working standards for that day's injections into the chromatograph. Dilutions of these final mixtures were with a solution of 3.5 m*M* Na_2CO_3–2.0 m*M* $NaHCO_3$. This buffer was utilized to stabilize the solutions and improve chromatography. Working standards were prepared and analyzed in random order. Concentration ranges for these final solutions were 56 to 68 ppm for fluoride, and 199 to 244 ppm for acetate; these working standards represented actual concentrations of 6.975 to 8.525% (w/w) for fluoride and 24.93 to 30.47% (w/w) for acetate. Peak areas were large enough to assure that any variability in the integration's stop-start points was negligible. Lower ranges (still in the 1:4 ratio) did not effect better resolution of the peaks.

A Sartorius LC 3201D analytical balance was used to prepare all the stock and intermediate standards. This balance was used because it was in an acid hood; masses were recorded to three decimal places. The working standards (weighings to four decimal places) were made on a Sartorius MC1 analytical balance.

Dilution errors in the daily working standards were estimated by conducting a Monte Carlo simulation. This exercise was based on the upper bounds on the magnitude of weighing error for the scales (0.001 g for the LC Balance and 0.0001 g for the MC1

Balance). In the simulation, weighing errors were randomly drawn from a Normal distribution with mean equal to zero and standard deviation equal to the upper bound. The distribution of these relative concentration errors was found never to exceed 0.1% relative error, which was considered negligible.

2.4. Stability of stock standards

Since both hydrofluoric and acetic acids are volatile, a stability study was conducted on the stock standards (the only ones not remade daily). No mixed solutions were made; acetic acid and HF were evaluated separately. For each, triplicates of the stock standard were prepared as above; these solutions were left undisturbed for five days before testing them. On the analysis day, these three standards were chromatographed along with three stock standards that were prepared immediately before analysis.

The new and old stocks were tested in alternating order, beginning with the new. When it was time to analyze each stock, a 2:100 dilution was made; from this solution, a mid-level working standard was prepared immediately, in quadruplicate. These four final solutions then were measured, using the 2.5 m*M* Na_2CO_3–3.4 m*M* $NaHCO_3$ eluent.

For each acid, the twelve raw peak areas were averaged for both the old and the new stocks. For fluoride, the R.S.D. values were 0.17% and 0.40%, respectively, indicating little variability over the course of a day. When Student's *t*-test was performed on the averages, the *p*-value was 0.4832, showing no evidence that the two means were different. Thus, no stability problems were evident for fluoride. For acetate, the R.S.D.s for each mean were 0.57% and 0.85%, respectively; again, variability within a day was not an issue. However, the mean for the old was approximately 1.0 relative % higher than for the new; the *p*-value for the *t*-test was 0.0032, indicating that there was a significant difference between the two. A possible explanation is that, with time, the solution picked up a slight amount of acetate from the plastic cup. Therefore, if a particular acetate analysis demands extremely high accuracy, that stock should be prepared as often as every day. Since standards were prepared the same way throughout this research, the slight stability issue for acetate would affect all calibration data equally. Therefore, it was deemed acceptable to use the same stock standard throughout the study.

3. Results and discussion

3.1. Calibration curves: General

In the author's laboratory, a commonly seen fluoride-to-acetate ratio was 7.75:27.7; these values were chosen for this study because they approximate the relative amounts in the Dionex test chromatogram [15]. In order to test calibration plots adequately for curvature, nine levels of standards were prepared for each acid; exact values are discussed in Fig. 1. Calibration results are discussed in detail in the following sections and are summarized in Tables 1 and 2.

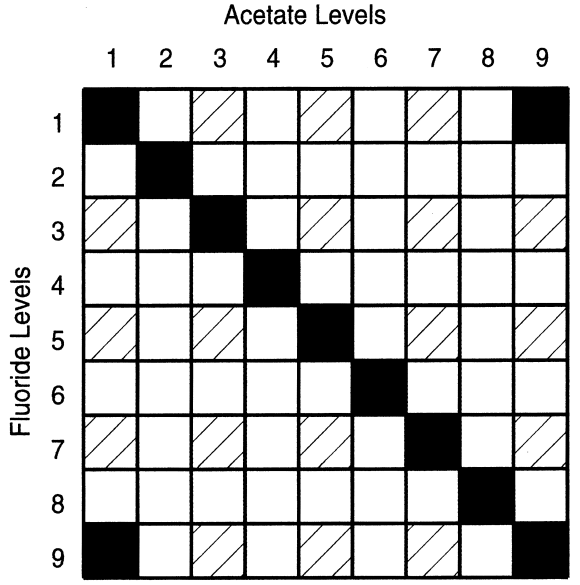

Fig. 1. Combinations of working-standard levels analyzed. Solid squares=mixtures tested each day. Hatched squares=mixtures tested on half of the days. Open squares=not used. Level 1 was prepared using 3.6 g of intermediate standard and diluting to 100 g with eluent. Subsequent levels were made by increasing the amount of intermediate by 0.1 g for each unit rise in level. Thus, level 5 required 4.0 g and level 9 required 4.4 g of intermediate. In the calibration curves, these ranges (in %, w/w) represented 6.975 to 8.525 for fluoride and 24.93 to 30.47 for acetate; mid-points were 7.75 and 27.7% (w/w), respectively.

Table 1
Calibration results for fluoride

Eluent	Number of points in curve	Peak area or height?	95% c.i. (%, w/w)	Adjusted r^2	Data used for curve
Strong	36	Area	±0.06	0.9966	4 replicates of the 9 'diagonal' levels (Fig. 1)
Strong	36	Height	±0.12	0.9856	4 replicates of the 9 'diagonal' levels (Fig. 1)
Weak	54	Area	±0.04	0.9982	6 replicates of the 9 'diagonal' levels (Fig. 1)

The various calibration curves came from two calibration studies, one for each eluent strength. See Section 3 for a detailed description of each curve.

3.2. Calibration curves: 2.5 mM Na_2CO_3–3.4 mM $NaHCO_3$ eluent

Various m*M* ratios of carbonate to bicarbonate (e.g., 2.5–3.4, 3.5–1.0, 1.0–0) were investigated. None gave baseline separation of fluoride and acetate. The ratio of 2.5 m*M* Na_2CO_3–3.4 m*M* $NaHCO_3$ was chosen for this study because it worked well for all the sample types analyzed in the author's laboratory. A typical chromatogram for a mid-level standard is shown in Fig. 2. Total run time was 3 min and peak shapes were not skewed dramatically.

Because the resolution was not complete, the amount of one analyte could affect the response of the second. For example, the peak area for a given level of acetate could depend on the amount (i.e., level) of fluoride that also was in the standard. To account for this possibility, a variety of standard

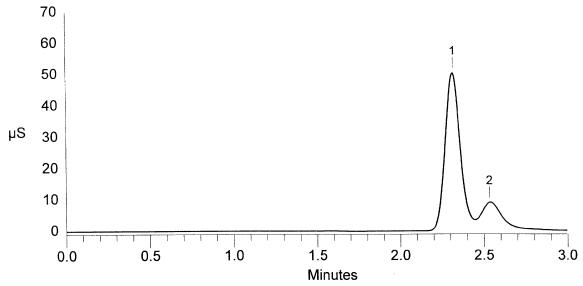

Fig. 2. A chromatogram of: (1) fluoride (7.75%, w/w), and (2) acetate (27.7%, w/w), where eluent is 2.5 m*M* Na_2CO_3–3.4 m*M* $NaHCO_3$.

Table 2
Calibration results for acetate

Eluent	Number of points in curve	Peak area or height?	95% c.i. (%, w/w)	Adjusted r^2	Data used for curve
Strong	36	Area	±0.74	0.9632	4 replicates of the 9 'diagonal' levels (Fig. 1)
Strong	80	Area	±1.0	0.9346	All available data
Strong	80	Area	±0.75	0.9682	All available data; fluoride concentrations= second *x*-term
Strong	36	Height	±1.65	0.8520	4 replicates of the 9 'diagonal' levels (Fig. 1)
Strong	80	Height	±1.75	0.8356	All available data
Strong	80	Height	±1.68	0.8562	All available data; fluoride concentrations= second *x*-term
Weak	54	Area	±0.41	0.9869	6 replicates of the 9 'diagonal' levels (Fig. 1)

The various calibration curves came from two calibration studies, one for each eluent strength. See Section 3 for a detailed description of each curve.

combinations was tested (see Fig. 1) [16]. Over a period of four days, a total of 80 data points was collected for each ion.

The desired calibration curve was a nine-level one where corresponding levels (e.g., level 3 for each ion) were mixed together. These standards were easy to prepare, and nine levels covered the range of interest sufficiently. Thus, these 36 points were selected from the full set of data. For fluoride, the model was adequate; adjusted r^2 was 0.9966 and the *p*-value was 0.7165 for the lack-of-fit test. (This latter number should be greater than 0.05; otherwise, the model is not adequate.) In addition, the 95% confidence interval (hereafter called '95% c.i.') was ±0.06% (w/w). This equation was applied to all 80 analyses; on average, the mean absolute deviation (i.e., the average of the absolute values of the quantities 'actual concentration minus predicted concentration') was 0.02% (w/w).

The situation was worse with acetate. Even on a daily basis, precision was poor compared with that seen in the stability study; for replicates of a given level, R.S.D. values were typically between 1.2 and 2.1%. Furthermore, the desired, nine-level curve for acetate was not as well behaved. The lack-of-fit test did show the model to be adequate (*p*-value= 0.6916), but adjusted r^2 was 0.9632 and the 95% c.i. was ±0.74% (w/w). When this curve was applied to all 80 data points, the mean absolute deviation was 0.39% (w/w). To try to improve the acetate situation, all 80 analyses were used to generate a curve. Here, the lack-of-fit *p*-value was 0.5530, adjusted r^2= 0.9346, the 95% c.i.=±1.0% (w/w), and the mean absolute deviation was 0.41% (w/w). A third curve was investigated to incorporate any influence of the fluoride concentration on the acetate response. This plot was formed using two *x*-variables (the concentration of acetate as well as that of fluoride) and one *y*-variable (peak area for acetate). The lack-of-fit *p*-value was 0.7504 and adjusted r^2 was 0.9682. The 95% c.i. and mean absolute deviations were ±0.75% (w/w) and 0.25% (w/w), respectively.

Peak heights were examined to see their effects in the calibration designs used above. In all cases, the straight-line model was adequate. With fluoride, adjusted r^2 fell to 0.9856 and the 95% c.i. rose to ±0.12% (w/w). For acetate, adjusted r^2 was never better than 0.8562 and the 95% c.i. rose to at least ±1.65% (w/w). These data indicated that peak areas afforded curves with better fit and better precision than did peak heights.

3.3. Calibration curves: 0.1 mM Na_2CO_3–0.1 mM $NaHCO_3$ eluent

To see the effect of baseline separation on the calibration curves, an eluent mixture was found that would resolve the peaks in as little time as possible. This task could not be accomplished with buffers above 1.0 m*M* each; a solution of 1.0 m*M* sodium carbonate almost resolved the two anions, but overlap still remained. The combination of 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$ accomplished the goal, with a run time of approximately 14 min. However, both peaks fronted severely (see Fig. 3).

The same standards matrix (see Fig. 1) was used as before. To incorporate as much variation as possible into the system, the solutions were analyzed over a period of six days, giving a total of 120 data points per anion.

For the curves, the nine same-level concentrations from above were used. The results for fluoride were similar to the above: lack-of-fit *p*-value=0.8939, adjusted r^2=0.9982, and 95% c.i.=±0.04% (w/w); the mean absolute deviation=0.02% (w/w) when the equation was applied to all 120 chromatograms. Acetate, on the other hand, demonstrated improved statistics of 0.9992, 0.9869, ±0.41% (w/w) and 0.17% (w/w), respectively.

After work was completed with this eluent, the chromatograph was used with the stronger buffer for other work. Subsequently, the instrument was shut

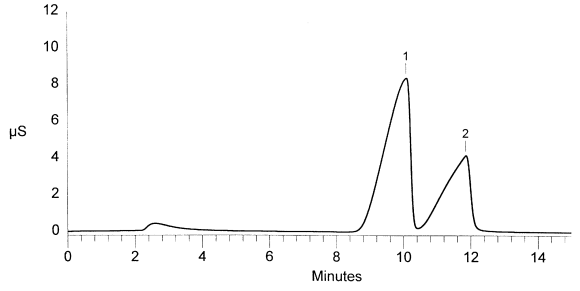

Fig. 3. A chromatogram of: (1) fluoride (7.75%, w/w), and (2) acetate (27.7%, w/w), where eluent is 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$.

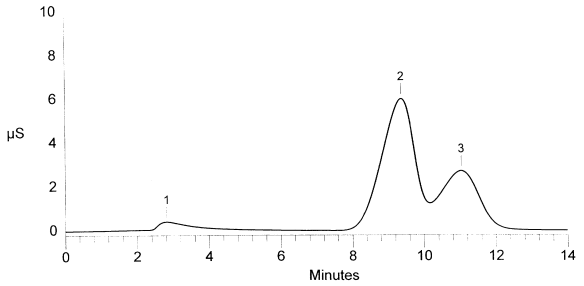

Fig. 4. A chromatogram of: (1) fluoride (7.75%, w/w), and (2) acetate (27.7%, w/w) after the column chromatography had shifted (eluent is 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$). See text for details.

down and moved to a new location. When the channel was used again with the 0.1 m*M* Na_2CO_3–0.1 m*M* $NaHCO_3$ eluent, the two peaks had merged slightly and had better shapes, as shown in Fig. 4. To make a rough assessment of the calibration curves under these conditions, the entire 29-point design (Fig. 1) was prepared and analyzed once, in random order. For each anion, all results were used to generate a least-squares curve. The straight-line model still was adequate for both plots. Adjusted r^2 was 0.9987 for fluoride and 0.9914 for acetate; 95% confidence intervals were ±0.04% (w/w) and ±0.35% (w/w), respectively; all of these results agreed well with those from the initial weak-eluent work. To compare these results with similar curves from the strong eluent, the latter's data were divided into separate days and individual plots were generated. The best 95% confidence intervals were ±0.03% (w/w) for fluoride and ±0.9% (w/w) for acetate; for adjusted r^2, the highest values were 0.9990 and 0.9573, respectively. Although these data are limited, they indicate that the weaker eluent is still the one of choice if high accuracy is needed for acetate.

4. Conclusions

Calibration results are summarized in Tables 1 and 2. Statistical comparison of the fluoride calibration curves showed similar results for both eluents. For acetate, though, a narrower confidence interval resulted with the weaker mobile phase. With it, a simple nine-level calibration curve had good statistical performance (high adjusted r^2 and narrow c.i.) and revealed no dependence on the amount of fluoride in the sample. However, peak shapes were distorted and run times were longer. The stronger eluent provided fast run times and well-behaved peak shapes. Even on a daily basis, though, acetate's precision suffered for a given level. Furthermore, high adjusted r^2 and a narrow c.i. could not be achieved even when the fluoride concentrations were added to the calibration model. As the column aged, the resolution deteriorated with the weak buffer, but the calibration data for both anions maintained the high fit and high precision seen earlier with this eluent.

Knowledge of these figures of merit allows the researcher to decide which situation is more appropriate for his or her analyses. It is possible to quantify both acetate and fluoride on the AS14 using a carbonate–bicarbonate eluent. If short analysis times and/or Gaussian peak shapes are required, a ratio similar to the vendor-recommended one will be needed. To achieve the best fit and best precision for the acetate calibration curve, though, a weaker mix (such as the one employed here) should be tried.

5. Terms used

95% Confidence interval (or 95% c.i.): a pair of confidence limits (an 'upper' and a 'lower') used to bracket the true value of a statistic. Here, 95% of all such intervals do contain the true value.

Intermediate standards: 2:100 g dilutions of the stock standard.

Level: the concentration of a standard.

Mean absolute deviation: the mean of the absolute values of the quantities 'true minus predicted'.

% (w/w): a concentration unit. It is the weight–weight percentage of a species in a final solution.

Relative %: the quantity 'true minus predicted', divided by the true and multiplied by 100.

Stock standards: solutions (7.75%, w/w, for fluoride and 27.7%, w/w, for acetate) made directly from concentrated Baker acids.

Working standards: solutions made from intermediate standards and used for analysis on the ion chromatograph (see Fig. 1 for exact values used).

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