*Journal of Chromatography*, 387 (1987) 301–312
Elsevier Science Publishers B.V., Amsterdam — Printed in The Netherlands

CHROM. 19 097

# DETERMINATION OF IODIDE AND THIOSULFATE BY PAIRED-ION, REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY WITH ULTRAVIOLET ABSORBANCE, ELECTROCHEMICAL, AND CONDUCTIMETRIC DETECTION*

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(First received May 5th, 1986; revised manuscript received September 25th, 1986)

## SUMMARY

Inorganic anions are typically determined by ion chromatography, ion-selective electrodes, or by "wet chemical" procedures. An alternative to these approaches is afforded by paired-ion, reversed-phase high-performance liquid chromatography (HPLC), and the application of this technique to the determination of iodide and thiosulfate is discussed. Each analyte can be determined using ultraviolet (UV) absorbance detection and oxidative, amperometric electrochemical detection (ED). Furthermore, in the case of iodide, an additional and quite selective ED scheme is available through the use of series-configured dual glassy carbon electrodes. The dual-series ED approach utilizes an upstream electrode wich is maintained at an oxidative potential. This results in the formation of an electroactive species, which may be detected at a downstream electrode held at a reductive potential. Finally, it is demonstrated that non-suppressed conductimetric detection is also perfectly viable within the context of paired-ion, reversed-phase HPLC, provided the overall conductance of the mobile phase is not excessive.

## INTRODUCTION

The development of ion chromatography represented one of the most significant advances in modern analytical chemistry. As originally described by Small *et al.*[1], this technique employed two resin-based, ion-exchange columns (one to achieve separation, plus a second for chemical suppression), along with conductimetric detection. Single-column ion chromatography (SCIC), which uses either silica or resin-

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0021-9673/87/$03.50 

based separation columns in conjunction with low-conductivity eluents, was developed shortly thereafter, and for some time was the only alternative to chemically suppressed ion chromatography[2]. SCIC sought to minimize the disadvantages inherent in suppressed ion chromatography, *e.g.*, post-column dead volume and resultant loss in system efficiency (due to the presence of the suppression column), the need for periodic regeneration or replacement of the suppression column, and restricted choices for eluents. By eliminating chemical suppression, however, SCIC generally provided less sensitivity than the original technique.

Paired-ion, reversed-phase high-performance liquid chromatography (HPLC) provides an additional means of separating inorganic anions. This was demonstrated by Reeve[3], who achieved successful chromatography for several anions using hexadecyl (cetyl) trimethylammonium bromide as an ion-pairing reagent along with a cyano-bonded, silica-based reversed-phase column and UV absorbance detection. Chiu[4] reported the determination of ethyl sulfate in the presence of inorganic sulfate and phosphate using refractive index (RI) detection and a chromatographic system consisting of a $C_{18}$ reversed-phase column and a mobile phase of 0.01 *M* tetrabutylammonium perchlorate in 30% methanol. By employing mobile phases based on either heptyl sulfate or tetrabutylammonium hydroxide, a $C_{18}$ reversed-phase column, and either conductimetric or UV absorbance detection, Molnar *et al.*[5] achieved separation of various anions and cations.

This general approach to the chromatography of inorganic anions offers a number of advantages over "classical" ion chromatography. In the first place, microparticulate reversed-phase columns provide greater chromatographic efficiencies than silica or resin-based ion-exchange columns. In addition, there is no need to purchase costly special-purpose, ion-exchange columns, which are often as much as five times as expensive as commercially available, high quality, bonded reversed-phase columns. Finally, an investment in extra chromatographic instrumentation is often unnecessary, since these separations can typically be performed using conventional HPLC systems. Since the appearance of the first reports describing this technique, numerous articles have been published citing the use of bonded, reversed-phase columns and paired-ion mobile phases for the determination of inorganic anions with detection based on conductimetric, UV, UV–VIS/indirect photometry, and electrochemistry[6–24].

The focus of this paper is the analysis of iodide and thiosulfate using a silica-based, microparticulate, $C_{18}$ bonded, reversed-phase column, and a mobile phase consisting of 0.005 *M* tetrabutylammonium hydrogen sulfate (TBAHS) dissolved in a solution of methanol–phosphate buffer (15:85), pH = 7.0. Detection was achieved by UV absorbance, direct (oxidative) amperometric electrochemical, or series-configured dual electrode, amperometric electrochemical detection (ED). In addition, both iodide and thiosulfate were determined using conductimetric detection with a mobile phase of 0.9 m*M* tetrabutylammonium salicylate dissolved in methanol–water (10:90).

## EXPERIMENTAL

### *Apparatus*

A modular HPLC system was assembled using, as components, a Waters Chro-

matography Division (Millipore, Milford, MA, U.S.A.) Model 6000A solvent delivery system, a Rheodyne (Cotati, CA, U.S.A.) Model 7125 syringe loading injector, and a Spectra-Physics (San Jose, CA, U.S.A.) SP4270 recording integrator. Detectors employed included the Kratos (Ramsey, NJ, U.S.A.) Spectroflow 757 variable-wavelength UV–VIS detector, the Bio-Rad (Richmond, CA, U.S.A.) Model CM-8 high-performance conductivity monitor, and the Bioanalytical Systems (West Lafayette, IN, U.S.A.) electrochemical detector, consisting of two Model LC-4B amperometric controllers and a Model TL-5A thin-layer transducer. Specific subcomponents of the Model TL-5A included a Model RE-1 Ag/AgCl reference electrode, a Model TG-5M 0.127-mm gasket, and dual glassy carbon electrodes. The chromatographic column used was an Alltech Assoc. (Deerfield, IL, U.S.A.) Econosphere $C_{18}$ reversed-phase column, 25 cm × 4.6 mm I.D.

*Mobile phase*

The primary mobile phase used was 0.005 *M* TBAHS dissolved in methanol–phosphate buffer (15:85). The specific phosphate buffer employed consisted of an aqueous mixture of 8.70 m*M* potassium dihydrogen phosphate and 30.4 m*M* disodium hydrogen phosphate. Final pH of the mobile phase was approximately 7.0. Prior to use, the mobile phase was aspirated through a Rainin Instruments (Woburn, MA, U.S.A.) 0.45-$\mu$m membrane filter and degassed under vacuum.

A second mobile phase, prepared specifically for use with the conductivity monitor, consisted of 0.9 m*M* tetrabutylammonium salicylate dissolved in methanol–water (10:90). The ion-pairing component was produced by combining an appropriate amount of salicylic acid with the corresponding volume of a suitably diluted solution of tetrabutylammonium hydroxide, such that the final concentration in the mobile phase was approximately 0.9 m*M*. Final pH of this mobile phase was 5.0, and, prior to use, it was filtered and degassed as above.

Our use of a suitable guard column, as well as a silica saturation pre-column, has served to extend the usable lifetime of analytical columns and to perform analyses upon complex sample matrices.

*Chemicals*

Solvents used to prepare mobile phases were deionized–distilled water and HPLC-grade methanol from Fisher Scientific (Fairlawn, NJ, U.S.A.). Ion-pairing reagents of the highest purity available were obtained from Fluka (Hauppauge, NY, U.S.A.). Reagent grade standards (Fisher) of potassium iodide and sodium thiosulfate were used for routine investigational studies. For quantitative determinations, high-purity standards were procured from Alfa Products, Thiokol/Ventron Division (Danvers, MA, U.S.A.).

*Procedures*

Authentic mixtures of potassium iodide and sodium thiosulfate were prepared and analyzed in single blind studies. Initial dilutions were made with deionized–distilled water. Further dilutions were made with mobile phase. Results from four such studies are presented in this paper. One or more of the following detection schemes were employed: (1) UV absorbance; (2) oxidative, amperometric electrochemical; (3) dual-series electrochemical (oxidative/upstream, reductive/downstream potentials); and (4) conductimetric.

In addition, a sample of enteric coated United States Pharmacopoeial potassium iodide tablets was assayed for iodide by HPLC using three distinct modes of detection. Twenty tablets were ground manually to pass through a 60-mesh sieve in order to form a composite. Sample preparation for HPLC involved initial dilution of a portion of the composite with deionized–distilled water, followed by filtration and final dilution with mobile phase. Recovery studies were performed by spiking the sample preparation with standard.

## RESULTS AND DISCUSSION

### *UV and ED optimization*

Both iodide and thiosulfate have UV spectra and are electrochemically active at a glassy carbon electrode surface. The behavior of these two species was characterized by obtaining UV absorbance spectra, cyclic voltammograms, and hydrodynamic voltammograms. Absorption maxima of approximately 212 nm and 223 nm were observed for thiosulfate and iodide, respectively. Cyclic voltammograms indicated that both analytes could be electrochemically oxidized at a glassy carbon surface. Hydrodynamic voltammograms confirmed this and indicated that usable signal responses could be generated for both species at about +0.8 V or above. Iodide and thiosulfate can also be oxidized at gold or platinum electrode surfaces, both of which are commercially available. However, neither surface was found to offer distinct advantages over glassy carbon, and all data presented was obtained with this electrode material.

Tetrathionate represents a potential degradation product in aqueous solutions of thiosulfate, as suggested by a referee. This species has a UV signal response at 212 nm which, under actual chromatographic conditions, is comparable to the parent compound. It elutes after both iodide and thiosulfate, subject to the experimental parameters used in this study. Typical retention times, at a flow-rate of 1.0 ml/min, for thiosulfate, iodide, and tetrathionate, were 3.2, 4.7, and 11.3 min, respectively. At a potential of +1.15 V tetrathionate's electrochemical, response is only 5–10% of that for a comparable solution of thiosulfate (10 ppm each). UV detection would therefore most likely be the method of choice for monitoring levels of tetrathionate. Following the conversion of thiosulfate to tetrathionate over time was not a primary objective of this study. Our main concern was that no extraneous peaks were present during a particular analysis, and indeed that was consistently the case with all samples analyzed here.

In addition to being oxidizable at a single fixed potential, iodide (but *not* thiosulfate) will yield a reductive response when a series-configured dual electrode transducer is used (Figs. 1 and 2). The reduction observed in a dual-series configured system proved to be a reliable, reproducible, and selective detection scheme. Linearity data have been compiled for iodide and thiosulfate using the UV detection and ED modes (Table I). These results suggest that paired-ion, reversed-phase HPLC represents a viable analytical approach to the determination of iodide and thiosulfate. Either anion may be determined at low levels (ppb)*, and signal responses are linear

* Throughout this article the American billion ($10^9$) is meant.

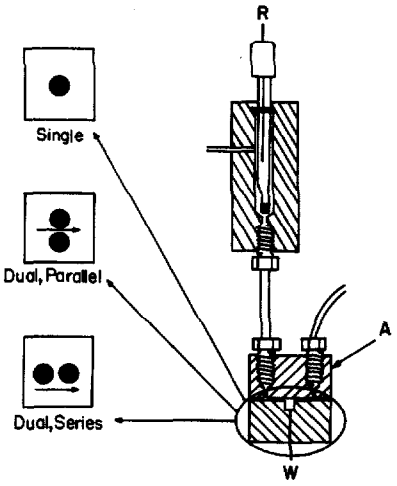



Fig. 1. Single and dual electrode transducer schematic: R = reference electrode; A = auxiliary electrode; and W = single, dual-parallel or dual-series working electrodes. Note that mobile phase enters through A, passes across W, and exits past R.

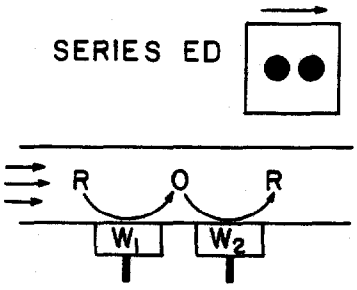



Fig. 2. Schematic of dual-series glassy carbon electrodes for determination of iodide. $w_1$ = +1.05 V (upstream electrode), $w_2$ = −0.15 V (downstream electrode). Note that oxidative signal produced at $w_1$ may be monitored and used for quantitation also.

over at least two orders of magnitude for all three detection modes employed, viz., UV, oxidative ED, and dual-series ED (iodide only).

While ED did not offer a marked advantage over UV in terms of sensitivity, it did provide a greater measure of selectivity than can be achieved with a conventional (i.e., non-scanning), single-channel UV detector. This selectivity is realized through the use of a parallel-configured dual electrode transducer. With the electrodes arranged in this manner, response ratios can be characteristic of each anion.

TABLE I

LINEARITY OF RESPONSE FOR IODIDE AND THIOSULFATE BY UV ABSORBANCE, DIRECT OXIDATIVE ELECTROCHEMICAL, DUAL-SERIES ELECTROCHEMICAL, AND CONDUCTIMETRIC DETECTION

See Figs. 4 and 5 for experimental conditions. Concentrations expressed as ppm. MDL = Minimum detection level. Minimum of three replicate injections used to determine data points.

| *Anion* | *Detection* | *Equation line* | *Correlation coefficient* | *MDL (ppb)* |
|---|---|---|---|---|
| $I^-$ | UV (223 nm) | $AU = 0.0189[I^-] - 3.82 \cdot 10^{-4}$ | 0.9999 | 10 |
| $S_2O_3^{2-}$ | UV (212 nm) | $AU = 0.00738[S_2O_3^{2-}] + 1.24 \cdot 10^{-4}$ | 0.9999 | 50 |
| $I^-$ | ED (+1.05 V) | $nA = 83.8[I^-] - 0.68$ | 0.9999 | 40 |
| $S_2O_3^{2-}$ | ED (+1.05 V) | $nA = 187.9[S_2O_3^{2-}] + 1.61$ | 0.9998 | 10 |
| $I^-$ | ED (−0.15 V) | $nA = 37.57[I^-] - 2.45$ | 0.9999 | 50 |
| $I^-$ | Conductimetric | $\mu S/cm = 0.1768[I^-] + 3.35 \cdot 10^{-2}$ | 0.9985 | 100 |
| $S_2O_3^{2-}$ | Conductimetric | $\mu S/cm = 0.2898[S_2O_3^{2-}] + 5.74 \cdot 10^{-2}$ | 0.9971 | 100 |

This is accomplished by setting the two electrodes at different potentials, typically 100–150 mV apart from one another. In many cases, this ratio is also constant over a range of concentrations.

The repeatability of the oxidative response at a single, fixed concentration for both iodide and thiosulfate was found to be quite stable at the two potentials ($w$) employed, *i.e.*, iodide (4.874 ppm); $w_1$ = +1.050 V, relative standard deviation (R.S.D.) = 0.98%, $w_2$ = +1.150 V, R.S.D. = 0.80%, R.S.D. of $w_2/w_1$ = 0.51%; thiosulfate (1.856 ppm); $w_1$ = +1.050 V, R.S.D. = 0.96%, $w_2$ = +1.150 V, R.S.D. = 1.3%, R.S.D. of $w_2/w_1$ = 1.17%. The respective response ratios, $w_2/w_1$, also proved to be repeatable. It is noteworthy in this regard that two to three injections of a concentrated (approximately 200 ppm of each anion) mixture of iodide and thiosulfate apparently served to precondition the electrode and thus permit maximum repeatability of response. Preconditioning with high concentrations may equilibrate the electrode more rapidly and effectively in a shorter period of time than repeated injections at low concentrations.

The stability of the analyte response ratios over a range of concentrations is summarized in Table II. The ratio for iodide is reasonably stable over a greater than two-fold concentration span (average values for the response ratio ranged from 1.2 to 1.3 with the R.S.D. = 3.0%). In the case of thiosulfate, a greater variation in response was observed as a function of concentration, with average response ratios ranging from 1.4 to 1.7 (R.S.D. = 7.4%). Since accepted analytical practice generally dictates that comparisons of standard and analyte be made at comparable concentration levels, and since response ratios for both iodide and thiosulfate have been shown to be reproducible at a particular concentration, the selectivity feature offered by current response ratios should still apply.

On the matter of selectivity, yet another degree of specificity (beyond that offered by response ratios) is possible in the case of iodide. While both iodide and thiosulfate are oxidizable at similar potentials on a glassy carbon surface, iodide will produce a downstream, reductive response as well as an upstream oxidative response

TABLE II

RESPONSE RATIOS ($i_2/i_1$) FOR IODIDE AND THIOSULFATE AS A FUNCTION OF CONCENTRATION OF SUBSTRATE

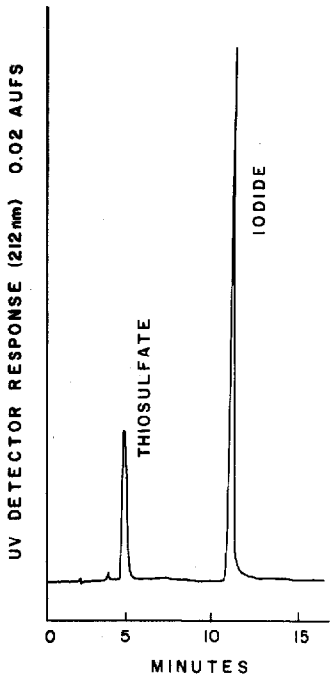
| *Anion* | *Concentration (ppm)* | $i_2/i_1$* | *R.S.D.** |
|---|---|---|---|
| Iodide | 4.793 | 1.28 | 0.40 |
| | 0.959 | 1.28 | 0.74 |
| | 0.192 | 1.24 | 0.90 |
| | 0.038 | 1.20 | 3.9 |
| Thiosulfate | 1.531 | 1.67 | 0.27 |
| | 0.306 | 1.53 | 0.24 |
| | 0.061 | 1.48 | 0.80 |
| | 0.012 | 1.40 | 1.9 |

* Average values for $i_2/i_1$ and relative standard deviation based on five injections at each concentration level.

when ED is carried out in a series-configured, dual electrode system. Thiosulfate does not exhibit such behavior under these conditions, *i.e.*, the oxidation product of thiosulfate does not undergo reduction at the downstream electrode. The "conversion efficiency" for iodide in the dual-series mode (*i.e.*, downstream signal response as a percentage of upstream signal response) was found to be on the order of 25–30%, which is in accordance with previous studies[25,26].

*Chromatography optimization*

Figs. 3 and 4 demonstrate the type of chromatography that can be realized by using the three detection techniques outlined above. These chromatograms are typical of those produced by a new column. The chromatogram in Fig. 3 is representative of results obtained using UV detection with the major peaks corresponding to thiosulfate and iodide, respectively. Fig. 4 depicts the two channels of signal response produced by a series-configured dual electrode system, with the upper chromatogram representing the response at the upstream, oxidative electrode, and the lower chromatogram representing the response at the downstream, reductive electrode.



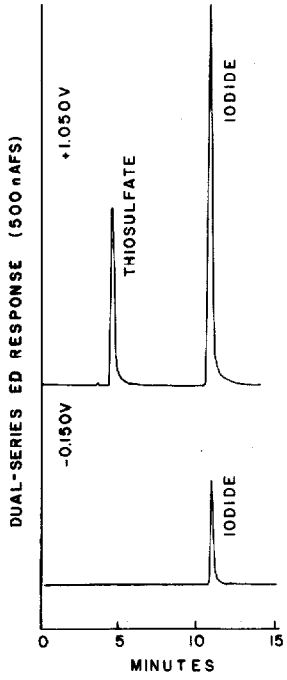




Fig. 3. Chromatogram of 1.531 ppm thiosulfate and 4.793 ppm iodide with UV detection (injection volume, 20 $\mu$l). Alltech Econosphere $C_{18}$ column, 25 cm × 0.46 cm I.D., mobile phase, 5 m*M* TBAHS dissolved in methanol–phosphate buffer (0.009 *M* $KH_2PO_4$, 0.03 *M* $Na_2HPO_4$) (15:85), flow-rate 1.0 ml/min.

Fig. 4. Chromatogram of 1.531 ppm thiosulfate and 4.793 ppm iodide with dual-series ED detection. $w_1$ = +1.05 V (upstream), $w_2$ = −0.15 V (downstream) *vs.* Ag/AgCl reference electrode. Additional conditions as in Fig. 3.

*Method validation*

Method validation was carried out by the determination of authentic mixtures of iodide and thiosulfate in single blind studies, and by the analysis of actual marketplace samples. In one instance, oxidative ED and UV detection were used to analyze a set of three authentic solutions containing both iodide and thiosulfate. Mean values were based on triplicate injections. The calculated values for iodide obtained using UV detection represented: 100.0% (R.S.D. = 0.21%), 101.9% (R.S.D. = 0.07%), and 100.3% (R.S.D. = 0.24%) of the actual values. With oxidative ED, the corresponding results for iodide were: 98.1% (R.S.D. = 0.19%), 101.0% (R.S.D. = 0.62%), and 100.1% (R.S.D. = 0.22%). For thiosulfate by UV detection, the percentages of actual value were: 98.5% (R.S.D. = 0.99%), 100.3% (R.S.D. = 0.16%), and 99.8% (R.S.D. = 0.12%), and by oxidative ED: 103.9% (R.S.D. = 0.32%), 102.6% (R.S.D. = 3.08%), and 100.0% (R.S.D. = 0.50%). Column effluent was routed first to the UV detector and then to the electrochemical cell.

A second set of authentics (now just with iodide) was evaluated, again observing the single blind protocol. The two detection methods employed were UV and dual-series ED, with only the downstream, reductive response monitored. Once again each detection scheme yielded calculated results which showed good agreement with actual values. Specifically, the percentages of actual value were: 99.6% (R.S.D. = 0.13%), 99.5% (R.S.D. = 0.17%), and 98.9% (R.S.D. = 0.17%), when UV detection was used, and 99.4% (R.S.D. = 1.01%), 100.2% (R.S.D. = 0.24%), and 99.0% (R.S.D. = 0.15%) with dual-series ED (reductive signal monitored). Dual series ED permits both iodide and thiosulfate to be quantitated through direct oxidative amperometric detection and offers, as well, a highly selective means of determining iodide by using the downstream, reductive response generated by that analyte.

*Enteric coated potassium iodide tablets.* A total of six discrete composite assays were performed on a sample of enteric coated potassium iodide tablets, USP (300 mg). Each assay was conducted making concurrent use of the three detection modes, *i.e.*, UV, dual-series ED with monitoring of both the upstream, oxidative signal and the downstream, reductive signal. A recovery study (spiking portion of sample preparation with known amount of standard) was performed for each assay. The resulting data has been compiled in Table III and evaluated statistically using the analysis of variance technique. The difference among the three detection modes was significant compared with experimental error. Specifically, oxidative ED provided significantly different values for mean iodide levels relative to either UV or reductive ED. Whereas no significant difference was observed for reductive ED *vs.* UV detection. These conclusions were based on application of the paired *t*-test[27]. Such a difference was not encountered with authentic solutions and may be attributable in this instance to the sample matrix itself. There was also a statistically significant difference among the portions of composite compared with experimental error. The physical nature of these tablets, specifically the presence of an enteric film coating surrounding the actual tablet formulation, did not permit a truly homogeneous composite to be realized. This fact may account for the variation in the reported results (*e.g.*, assays 1, 4, and 5). Nonetheless, all assays are within USP specifications of 94.0–106.0% of declaration, and the recovery data are quite consistent.

*Potassium iodide oral solution.* The only other USP monograph for an iodide

TABLE III

ASSAYS OF POTASSIUM IODIDE TABLETS, USP (ENTERIC) 300 mg

| *Detection* | | *Assay value** | *R.S.D.*** | *% Declared* | *Amount spiked* | *% Recovery* |
|---|---|---|---|---|---|---|
| (1) | Oxidation | 291.1 | 0.82 | 97.3 | 14.00 | 98.8 |
| | Reduction | 286.6 | 0.22 | 95.5 | 14.00 | 102.2 |
| | UV | 289.9 | 0.50 | 96.6 | 14.00 | 101.7 |
| (2) | Oxidation | 305.5 | 0.29 | 101.8 | 14.31 | 97.6 |
| | Reduction | 302.6 | 0.39 | 100.9 | 14.31 | 99.7 |
| | UV | 302.1 | 0.31 | 100.7 | 14.31 | 100.1 |
| (3) | Oxidation | 303.9 | 0.14 | 101.3 | 14.94 | 97.5 |
| | Reduction | 301.4 | 0.13 | 100.5 | 14.94 | 98.7 |
| | UV | 301.1 | 0.00 | 100.4 | 14.94 | 99.5 |
| (4) | Oxidation | 315.1 | 1.01 | 105.0 | 16.83 | 99.3 |
| | Reduction | 313.3 | 0.66 | 104.4 | 16.83 | 101.4 |
| | UV | 313.6 | 0.22 | 104.5 | 16.83 | 99.5 |
| (5) | Oxidation | 315.5 | 1.05 | 105.2 | 16.94 | 96.5 |
| | Reduction | 313.3 | 0.62 | 104.4 | 16.94 | 98.0 |
| | UV | 313.0 | 0.22 | 104.3 | 16.94 | 97.5 |
| (6) | Oxidation | 300.7 | 0.52 | 100.2 | 16.14 | 99.3 |
| | Reduction | 296.9 | 0.25 | 99.0 | 16.14 | 100.6 |
| | UV | 298.9 | 0.00 | 99.6 | 16.14 | 100.0 |

* Expressed as mg potassium iodide per tablet; USP specifications: 94.0–106.0% of declaration: each assay performed on a discrete portion of composite.

** Relative standard deviation based on triplicate injections.

formulation is potassium iodide oral solution. This product is simply an aqueous solution containing a very high concentration of potassium iodide (100 g per 100 ml) with sodium thiosulfate as an optional component at a proportion of only 0.5 mg per g of potassium iodide (*i.e.*, 0.05%). As has been described above, authentic solutions containing potassium iodide and sodium thiosulfate (in arbitrary proportions convenient for determination by HPLC) have been analyzed. A single blind study was performed on a set of authentic solutions which contained both anions in a ratio which is a replication of the USP formulation (*i.e.* potassium iodide at a level 2000 times that of sodium thiosulfate). This extreme disparity in analyte concentrations, and thus in respective detector responses, creates a much more difficult analysis. It should be noted that there is no requirement for quantitation of sodium thiosulfate in the USP monograph. Nonetheless, an attempt was made to estimate sodium thiosulfate under conditions reflecting an actual sample (see Table IV). Dual-parallel ED was employed with both oxidative signals being monitored.

The primary difficulty encountered in performing this analysis relates to the very large detector response produced by the iodide peak eluting several minutes after the thiosulfate peak. From a practical standpoint, one can: (a) simply wait for the detector output to return to a baseline level (as was done here); (b) place the

detector in standby prior to elution of the iodide peak (re-applying the original potential); or (c) activate a switching valve to divert column effluent to waste once the thiosulfate peak has eluted. Further refinement of this procedure was not deemed necessary for the purposes of this study, in view of the lack of any compendial requirement for determination of the sodium thiosulfate component of potassium iodide oral solution.

In this particular study, calculated values obtained from data generated with a detector setting of +0.95 V were more accurate than those obtained at +1.05 V. It might be premature to conclude that this is the preferred setting, however, in view of the relative standard deviations observed at each potential. The consistently lower values obtained at the +1.05 V setting was possibly due to the working electrode's reduced ability to recover from its initial response to a high iodide level. This "recoverability" or temporary passivation effect may be greater at +1.05 V than at +0.95 V, which could explain the data. Use of a switching valve would probably be the best choice if rigorous quantitation of thiosulfate in this sample matrix were necessary. The major objective here was to demonstrate that a reasonable estimation of the level of thiosulfate in this product could be obtained through the use of paired-ion, reversed-phase HPLC with ED, as Table IV indicates.

*Conductimetric detection*

We concluded this study by evaluating conductimetric detection for the determination of iodide and thiosulfate in a paired-ion, reversed-phase system. The mobile phase that was previously employed was modified slightly in order to create an eluent which would achieve separation of iodide and thiosulfate, yet not be so highly conductive as to preclude low levels of detection. Table I summarizes the linearity data obtained for the conductimetric detection of iodide and thiosulfate.

While analyte signal response could be successfully monitored at levels of approximately 100 ppb for each analyte, quantitation at these concentrations proved difficult due to poor reproducibility of peak response. Minimum detection limits of 100 ppb for both iodide and thiosulfate are therefore conservatively claimed for this system. With more thorough thermostatic control to limit baseline fluctuations, lower

TABLE IV

DETERMINATION OF THIOSULFATE IN PRESENCE OF LARGE EXCESS OF IODIDE

| *Authentic No.* | *Actual value** | *Detection* | *Calculated value* | *R.S.D.*** | *% of actual value* |
|---|---|---|---|---|---|
| 1 | 12.78 | $w_1$ = +0.950 V | 12.73 | 10.05 | 99.6 |
| | | $w_2$ = +1.050 V | 12.31 | 0.71 | 96.3 |
| 2 | 12.48 | $w_1$ = 0.950 V | 12.51 | 8.79 | 100.2 |
| | | $w_2$ = +1.050 V | 11.86 | 1.69 | 95.0 |
| 3 | 12.92 | $w_1$ = +0.950 V | 12.60 | 2.24 | 97.6 |
| | | $w_2$ = +1.050 V | 11.95 | 4.58 | 92.5 |

* Actual and calculated values expressed as mg of $Na_2S_2O_3 \cdot 5H_2O$ per 100 ml.

** Relative standard deviations based on triplicate injections.

detection limits should prove possible. Signal-to-noise was not the limiting factor. A representative chromatogram is indicated in Fig. 5 for the separation of iodide and thiosulfate with conductimetric detection. The elution order has been reversed (iodide elutes before thiosulfate) as a result of the modified eluent.

Consistent with approaches employed with UV detection and ED, single blind studies of authentic mixtures of iodide and thiosulfate were performed to assess the accuracy of the overall method. A set of three authentic solutions of potassium iodide and sodium thiosulfate was determined by conductimetric detection. For iodide, the calculated value represented 99.0% (R.S.D. = 2.84%), 99.7% (R.S.D. = 0.94%), and 100.4% (R.S.D. = 0.0%) of the actual values. The corresponding figures for thiosulfate were: 105.0% (R.S.D. = 0.50%), 100.4% (R.S.D. = 0.23%), and 101.8% (R.S.D. = 1.34%). Mean calculated values were based on triplicate injections. Although conductimetric methods proved to be perfectly viable within the context of paired-ion, reversed-phase HPLC, it did suffer slightly in comparison with UV detection or ED. In particular, the latter techniques exhibited better linearity and detection limits. An implicit advantage to conductimetric detection, of course, is its virtual universal applicability for all inorganic anions. UV detection and ED are inherently more selective, and hence less widely applicable techniques. It should be noted, however, that non-absorbing anions can still be quantitated *without* the use of a conductivity detector. Paired-ion mobile phases possessing inherent UV absorptivity can be prepared in order to achieve detection through "indirect photometry" or "UV–VIS". So-called "vacancy" peaks are created as the transparent sample bands elute from the column against a background absorbance resulting from the mobile phase[28–30].

Regardless of the detection scheme used, paired-ion, reversed-phase HPLC has proven to be a very effective approach to the analysis of inorganic anions, and it deserves serious attention and consideration as an alternative to the ion-exchange columns and eluents which are typically employed in "ion chromatography".

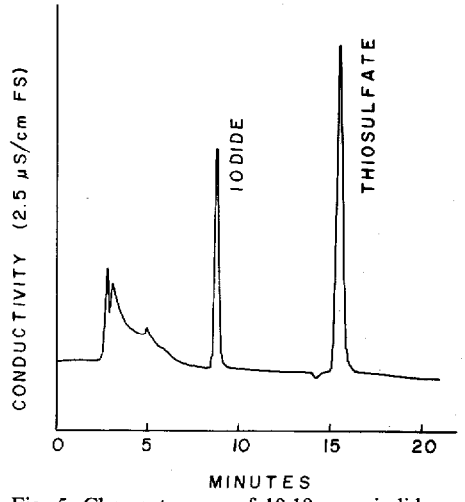



Fig. 5. Chromatogram of 10.19 ppm iodide and 9.784 ppm thiosulfate with conductimetric detection (injection volume, 20 µl). Alltech Econosphere $C_{18}$ column, 25 cm × 0.46 cm I.D., mobile phase 0.9 m*M* tetrabutylammonium salicylate dissolved in water–methanol (90:10), flow-rate 1.0 ml/min.

ACKNOWLEDGEMENTS

We wish to acknowledge the generous assistance of Boston District analysts Susan Krzysko and Kenneth Panaro, who prepared the authentic solutions used in this study. We are also grateful to Carl Selavka at Northeastern University, a doctoral candidate in the Chemistry Department and The Barnett Institute. He provided valuable suggestions on optimization of electrochemical detector performance. Finally, we wish to express our appreciation to the Science Advisor Research Associate Program (SARAP) Advisory Committee for endorsing this research program and to the U.S. Food and Drug Administration for providing the financial support that enabled the work to be conducted. We thank Ron Shoup and Peter Kissinger of Bioanalytical Systems, Inc. for technical assistance and information, and for permission to reproduce certain figures (Figs. 1 and 2).

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