

Sequential Flow-Injection Potentiometric Determination of Iodide and Iodine in Povidone Iodine Pharmaceuticals*

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ABSTRACT

A potentiometric sensor-based flow-injection system for determining iodide is described. The system utilizes a flow-through sandwich cell and incorporates iron (II)-tris bathophenanthroline iodide ion pair complex as an exchange site in a PVC matrix membrane. The sensor displays a fast response for 10^{-1} to 10^{-6} M iodide ion with an anionic slope of 59.1 ± 0.3 mV/concentration decade over the pH range 1 to 11. The experimental setup offers a precise, sensitive, selective and high sample throughput technique for determining iodide and iodine over a wide range of concentration. The limit of detection is 0.5 ppm iodide in a 20 μ L sample. The average recovery is 99.8%, and the mean standard deviation is 0.5%. Sequential flow-injection determination of iodide and iodine in some pharmaceutical preparations containing povidone iodine is performed by sample injection in a sodium sulfate-ascorbic acid stream and monitoring of the total iodide equivalent to I^- and I_2 . This is followed by injection of a second sample in an alkaline resorcinol stream and measuring of the iodide equivalent to I^- and $1/2 I_2$. Iodine and iodide concentrations are calculated from the consecutive signals. The method gives results in good agreement with those obtained by the United States Pharmacopeia.

KEY WORDS: Iron (II) bathophenanthroline iodide membrane, Iodide PVC sensor, Potentiometry, Sequential determination of iodine and iodide, Povidone iodine, Pharmaceutical analysis, Flow-injection analysis.

INTRODUCTION

Povidone iodine (2-pyrrolidinone, 1-ethenyl-homopolymer compound with iodine) is a loose complex of elemental iodine with povidone [1]. It contains not less than 9% and not more than 12% of available iodine which is bound to povidone as HI_3 and I_2 . It serves as a sustained release reservoir of iodine (iodophore) and is used as bacteriostatic, bactericidal, and antiseptic agents [2]. Methods described in the United States [3] and British [4] Pharmacopoeias for the assay of povidone iodine are based on visual iodimetric titration of the available iodine and argentimetric titration of the total iodide after reduction with sodium bisulfite. Potentiometric titrations have also been suggested with redox and iodide selective membrane electrode systems [5].

The construction and application of iodide ion selective electrodes for potentiometric determination of iodide ion in various matrices are well documented [6,7]. Liquid membranes consisting of long chain quaternary ammonium iodide in lipophilic solvents [8-11] and graphite rod coated with poly (3-methyl thiophene) iodide conducting polymer [12] have been proposed as

iodide sensors. Heterogeneous membranes have been based on aliquat iodide [13] nitron iodide [14] AgI [15], Ag-AgI [16], and Ag_2S -AgI [17,18] as electroactive materials dispersed in silicon rubber [14,15], epoxy resin [13,16,18], and methacrylate [17] matrices. Iodide sensing electrodes with homogeneous solid state Ag_2S -AgI membrane have been also described and thoroughly investigated due to their commercial availability [6,7]. These sensors vary widely in their sensitivity, working pH range, response time, influence of foreign ions, and potential stability. The studies reported to date with most of these sensors have been carried out mainly in the manual mode.

On the other hand, the use of the ISEs in flowing streams has grown rapidly [19]. Flow-through tubular iodide electrodes based on epoxy resin heterogeneous Ag_2S -AgI [20] and solid state Ag/AgI [21-23] membranes have been described for flow-injection determination of iodide. Adsorption problems at the electrode surface [21], influence of the iodide concentration added to the car-

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rier solution, and thickness, length, and conditions of the membrane [22,23] significantly affect the performance of these sensors. It may also be noted that in most of the reported flow-injection methods, the emphasis was placed on the determination of a single species in the sample. Little work has been published on the sequential or simultaneous determination of more than one species in the same sample; an approach which would make the flow-injection analysis concept more attractive for routine laboratories.

The present work describes construction and electrochemical evaluation of a novel poly (vinyl chloride) matrix membrane iodide sensor based on the use of iron (II)-tris bathophenanthroline iodide ion pair complex as an ion exchanger and 2-nitrophenyl phenyl ether as a plasticizing solvent mediator. This sensor offers the advantages of simplicity, selectivity, sensitivity, reliability, automation feasibility, remote sensing ability, low cost, and fast provision of analytical data. The incorporation of the proposed sensor in a flow-through sandwich cell provides an efficient flow-injection detector for determination of iodide. The assembly is used for sequential determination of I^- and I_2 in povidone iodine pharmaceuticals by consecutive injection of the sample in flowing streams of sodium sulfate-ascorbic acid and alkaline resorcinol. The limit of detection is $5 \mu\text{g } I^-/\text{mL}$, the precision is better than 0.8%, and the minimum throughput is 60 sample/h.

EXPERIMENTAL

Apparatus

Potentiometric measurements were performed at $25 \pm 1^\circ\text{C}$ using an Orion digital pH/mV meter (Model SA 720) and an iodide-PVC matrix membrane sensor in conjunction with an Orion Ag/AgCl single junction reference electrode (Model 90-01) filled with 10% w/v KCl. An Orion solid state $\text{Ag}_2\text{S}/\text{AgI}$ electrode (Model 94-06A) was used in some experiments for comparison with a double junction Ag/AgCl reference electrode containing 10% w/v KNO_3 in the outer chamber (Orion 90-02). A combination Ross glass pH electrode (Orion 81-02) was used for all pH measurements. A platinum redox electrode (Orion 96-78) was used for monitoring the iodimetric titrations.

The arrangement for the flow-injection analysis (FIA) system (Figure 1) consisted of a Manostat cassette pump (Junior, NY) and an Omnifit injection valve (Omnifit, Cambridge, UK) with sample loop of 20 μL volume. Tygon tubings (0.8 mm i.d.) and mixing coil (15 cm) were used. A laboratory-made sandwich flow-through iodide cell was used with an Orion 90-01 Ag/AgCl single junction reference electrode placed in a Petri dish down stream from the indicator cell just before the solution went to waste. The carrier and reagent streams were supplied from separate reservoirs. The potentiometric signals were monitored with an Orion SA 720 digital pH/mV meter and displayed in the form of peaks on a strip chart recorder (Linear 1200).

Reagents and Materials

All reagents were prepared from analytical reagent grade chemicals unless otherwise specified, and double distilled deionized water was used throughout. Bathophenanthroline (4,7-diphenyl-1, 10-phenanthroline, bphen), tetrahydrofuran (THF), and poly (vinyl chloride) powder were obtained from Aldrich Chemical Co. (Milwaukee, WI). 2-Nitrophenyl phenyl ether (NPPE) was purchased from Kodak (Rochester, NY). A 10^{-1} M stock solution of iodide was prepared and standardized by potentiometric titrations (iodometry using platinum redox electrode system and argentimetry using $\text{Ag}_2\text{S}/\text{AgI}-\text{Ag}/\text{AgCl}$ electrode system). Standard working solutions (10^{-2} to 10^{-6} M) were prepared by dilution of appropriate aliquots of the stock iodide solution with double distilled water. Pharmaceutical preparations containing povidone iodine (PI) were obtained from local drug stores.

Flow-Injection Solutions

Three carrier and reagent solutions were used: solution (A) consisted of a mixture of 5×10^{-2} M sodium sulfate and 2×10^{-2} M ascorbic acid; solution (B) consisted of 10^{-2} M aqueous resorcinol solution adjusted to pH 8.5 with sodium hydroxide; and solution (C) consisted of 10^{-1} M acetate buffer of pH 4.7. All these solutions were propelled through the FI system by means of a peristaltic pump at a flow rate 0.42 mL/min and Tygon tubings (0.8 mm i.d.).

Iron (II) Tris Bathophenanthroline Iodide Complex

A 0.1 g portion of 4,7-diphenyl-1,10-phenanthroline (bathophenanthroline) was dissolved in 20 mL of 95% v/v ethanol-water, and the solution was mixed with 1.0 mL of 0.1 M iron (II) ammonium sulfate. After stirring for 5 minutes, 5 mL of 0.1 M aqueous potassium iodide solution was added. A deep red precipitate of $[\text{Fe}(\text{bphen})_3] \text{I}_2$ was formed. The precipitate was filtered off on Whatman filter paper no. 42, washed with cold water, dried at room temperature for 24 hours, and ground to a fine powder. Elemental analysis and infrared data confirmed the formation of 1:2 iron (II) bathophenanthroline:iodide complex.

Iodide PVC Coated Disk Sensor

An electrode body was used which consisted of a silver disk (1 mm thick and 1.0 cm diameter) fixed to one end of Perspex tube using Araldite glue. A shielded cable was connected to the silver disk with silver epoxy resin. The other end of the tube was closed with a polyethylene cap. About 1 mL solution of the membrane cocktail (0.1 g PVC, 10 mg $[\text{Fe}(\text{bphen})_3] \text{I}_2$ and 0.4 g of 2-nitrophenyl phenyl ether in 6 mL of THF) was deposited dropwise on the silver disk. After each addition, the solvent was allowed to evaporate slowly at room temperature to give the first layer of membrane. This operation was repeated six times. The electrode was conditioned by soaking into 0.1 M KI solution for 1 hour and stored in the same

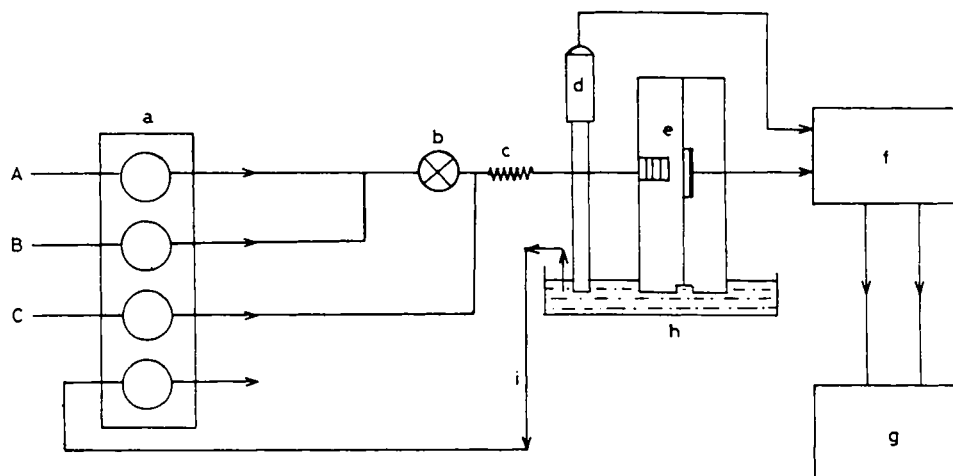


FIGURE 1. Flow-injection manifold for sequential determination of iodide and iodine using carrier solutions (A) 5×10^{-2} M Na_2SO_4 and 2×10^{-2} M ascorbic acid, (B) 10^{-2} M aqueous resorcinol adjusted to pH 8.5 with NaOH, and (C) 10^{-1} M acetate buffer of pH 4.7. The instrument components are (a) peristaltic pump, (b) injection valve, (c) 15-cm mixing coil, (d) Ag/AgCl single junction reference electrode, (e) flow-through sandwich iodide detector, (f) pH/mV meter, (g) strip chart recorder, (h) Petri dish, and (i) waste.

solution when not in use. This assembly was used for manual determination of iodide under static conditions.

The calibration of the electrode was carried out by placing it in conjunction with the single junction Ag/AgCl reference electrode in a 50 mL beaker containing 10 mL aliquot of 5×10^{-2} M Na_2SO_4 solution. Aliquots (1.0 mL) of 10^{-5} to 10^{-1} M standard potassium iodide solutions were successively added, and the potential readings were recorded after stabilization to ± 0.2 mV after each addition. The emf was plotted as a function of logarithmic iodide concentration.

Iodide Flow-Through Sandwich Cell

A flow-through sandwich potentiometric cell similar to that previously used [24,25] but equipped with an iodide PVC membrane was fabricated and utilized in the FI system. The membrane cocktail used for the coated disk sensor was deposited dropwise on the silver disk of the cell and allowed to evaporate at room temperature. The iodide sensor was conditioned by keeping the membrane in contact with 10^{-1} M KI for 10 hours. The cell was assembled and connected to the flow-injection system (Figure 1).

The potentiometric selectivity coefficients ($K_{1,B}^{\text{pot}}$) for the iodide sensor were measured by recording the signal height of $20 \mu\text{L}$ of 10^{-2} M solution of the interferences into a flowing stream of 5×10^{-2} M Na_2SO_4 solution. The potential response for iodide ion was obtained in a similar manner at the same concentration level. The selectivity coefficients were calculated using the method of Srinivasan and Rechnitz: [26]

$$-\log(K_{1,B}^{\text{pot}}) = (E_1 - E_2)/S$$

where E_1 and E_2 are the potential readings of signal heights observed for the same concentration of iodide

and interferences, respectively, and S is the slope of iodide calibration graph (mV/concentration decade).

Flow-Injection Determination of Iodide

A single line flow-injection system with a 5×10^{-2} M Na_2SO_4 carrier stream was used. The cell was assembled, connected to the system, and placed in conjunction with a single-junction Ag/AgCl electrode in a Petri dish filled with the carrier electrolyte solution. Successive $20 \mu\text{L}$ aliquots of 10^{-1} to 10^{-5} M standard iodide solutions were injected into the flowing stream using an Omnifit injection valve. The tubing distance between the injection valve and the detector was 10 cm. Both the iodide and reference electrodes were connected to an Orion 720 pH/mV meter which was attached to a strip-chart recorder to monitor the FI signals. The waste from the Petri dish was continuously removed by the peristaltic pump. At least three signals for each sample were recorded, and their average height or potential value was measured.

Flow-injection determination of iodide and/or iodine was similarly carried out using the carrier reagent (A). The signal heights or potentials were compared with a calibration plot made with 10^{-2} to 10^{-5} M potassium iodide solutions under the same conditions.

Sequential Flow-Injection Determination of Iodide and Iodine in Povidone Iodine Pharmaceuticals

Mouth wash, vaginal douche, and antiseptic PI solutions (1 to 10% w/v PI) were diluted 10 to 50 times before use with double distilled water. The carrier solution (A) was allowed to flow in the FI system. After baseline stabilization to ± 0.2 mV, $20 \mu\text{L}$ aliquots of PI samples were injected. At least three signals were recorded for each

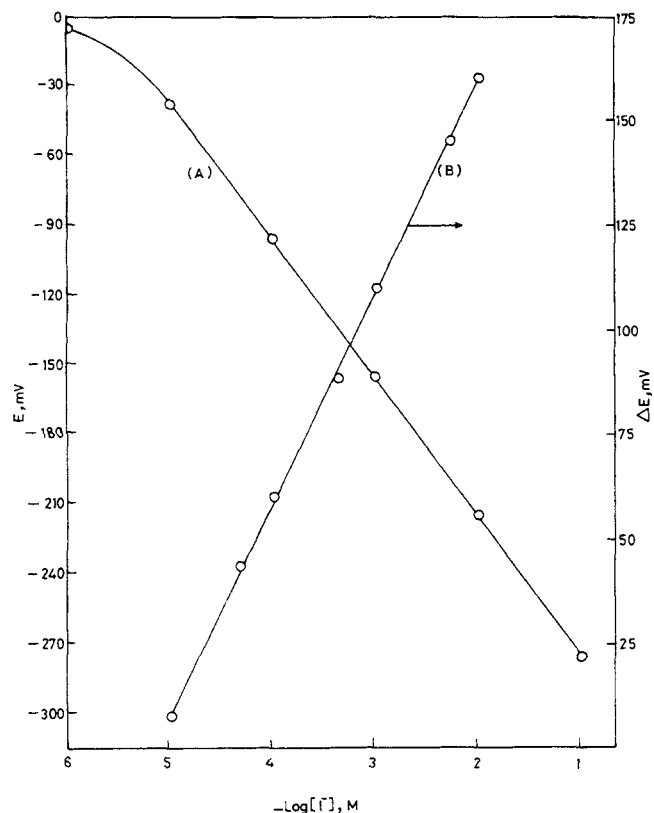


FIGURE 2. Typical calibration plot of iodide in 5×10^{-2} M Na_2SO_4 background (A) under static mode of operation using a coated disk iodide sensor and (B) under hydrodynamic mode of operation using a flow-through sandwich iodide detector.

sample, and the average height or mean potential was measured (signal a). Then the flow of the carrier solution (A) was stopped, and the carrier solutions (B) and (C) were propelled in the FI system. After baseline stabilization to ± 0.2 mV, $20 \mu\text{L}$ aliquots of the PI sample were injected and the average signal potential or height was measured (signal b). Iodine and iodide concentrations were calculated according to the relations

$$\text{Iodine concentration} \equiv 2 [(\text{signal a}) - (\text{signal b})]$$

$$\text{Iodide concentration} \equiv (\text{signal a})$$

$$- 2 [(\text{signal a}) - (\text{signal b})]$$

$$\equiv 2 (\text{signal b}) - (\text{signal a})$$

RESULTS AND DISCUSSION

Nature and Composition of the Iodide Sensor

Iron (II)-tris (4,7-diphenyl-1, 10-phenanthroline) cation reacts with iodide ion to form a water insoluble 1:2 ion-pair complex of the type $[\text{Fe}(\text{bphen})_3]_2\text{I}_2$. A silver disk (1 cm diameter) coated with a sensor cocktail of the composition 2:28:70% w/w $[\text{Fe}(\text{bphen})_3]_2\text{I}_2$, poly (vinyl chloride), and 2-nitrophenyl phenyl ether plasticizer, re-

TABLE 1 Response Characteristics of Iodide PVC Membrane

Parameter	Static with Coated Disk Electrode	Hydrodynamic with a Flow-Through Cell
Slope (mV/decade)	59.1 ± 0.3	50.1 ± 0.5
Correlation coefficient (r)	0.9998	0.9997
Intercept (mV)	330 ± 0.9	262 ± 0.7
Lower limit of linear range (M)	6×10^{-6}	10^{-5}
Lower limit of detection (M)	4×10^{-6}	10^{-5}
Response time for 10^{-4} M (s)	12	22
Recovery time (s)	25	30
Working pH range	1-11	1-11

spectively, was prepared and examined as an iodide ion membrane sensor. The electrochemical characteristics of the sensor were evaluated under static conditions and under hydrodynamic flow according to IUPAC recommendations [27] using the cell Ag // iodide PVC membrane // iodide test solution / Ag-AgCl reference electrode.

The linear response of the conventional configuration of the sensor under static conditions in 5×10^{-2} M sodium sulfate background covers the range of 6×10^{-6} to 10^{-1} M iodide with an anionic slope of 59.1 mV/concentration decade (Figure 2). The lower limit of detection is approximately $0.5 \mu\text{g I}^-/\text{mL}$. Least-squares analysis of the data gives the relation E (mV) = $(-59.1 \pm 0.3) \log [\text{I}^-] - (330 \pm 0.9)$. Figure 2 also shows a calibration plot obtained by injection of $20 \mu\text{L}$ of standard working iodide solutions in 5×10^{-2} M sodium sulfate carrier stream at the flow rate 0.42 mL/min via a single line manifold to the detector which consists of a flow-through sandwich iodide sensor. The peak heights in millivolts are plotted as a function of logarithmic iodide concentration. In the linear response range (10^{-5} to 10^{-2} M iodide), a slope of 50.1 mV/decade change in concentration is obtained. The lower limit of detection is $\sim 1.5 \mu\text{g I}^-/\text{mL}$. The least-squares analysis of the data gives the relation ΔE (mV) = $(-50.1 \pm 0.5) \log [\text{I}^-] - (262.2 \pm 0.7)$.

Table 1 summarizes the response characteristics of the iodide sensor under static and hydrodynamic conditions from data collected over a period of 3 months for five different sensor assemblies for each system. It can be seen that the dynamic linear response range under hydrodynamic mode of operation is slightly less than that obtained under the static conditions probably due to sample dilution. However, a working concentration range between 10^{-5} and 10^{-2} M iodide is easily achieved under hydrodynamic flow mode.

Response Time

The response time of the iodide sensor was tested for 10^{-1} to 10^{-5} M iodide solution. The sequence of measurements was from low to high concentration. The time

required for the sensor to reach values within ± 0.2 mV from the final equilibrium potential after increasing the iodide concentration level tenfold was measured. The response time is significantly short. It ranges from 10 seconds for $[I^-] \geq 10^{-4}$ M to 30 seconds for $[I^-] < 10^{-4}$ M.

The dynamic response time of the flow-through sandwich cell incorporating the proposed iodide detector was studied under low dispersion conditions by injection of standard solutions of potassium iodide in a flow stream of 5×10^{-2} M Na_2SO_4 . The time was recorded for the beginning of the variation of the baseline potential until it reached 98% of the maximum potential. The time for return to the baseline (recovery time) was also measured under the same conditions. The data obtained reveal fast response time and sample throughputs of about 60 samples/h. The interval between the start of the signal and its return to the baseline (Δt) which corresponds to the time taken by the sample to pass through the detector is significantly short. This indicates the suitable configuration of the proposed iodide PVC flow-through sandwich cell which permits a maximum contact area per unit volume and a minimum detector dead volume.

Response Stability

The potential displayed by the proposed iodide sensor for consecutive measurements of 10^{-1} to 10^{-5} M standard iodide solutions under static conditions in the same day does not vary by more than ± 1 mV ($n = 10$). Changes in the calibration slopes do not exceed ± 0.5 mV/decade change of iodide concentration. In order to confirm the long-term stability of the electrode response, it was tested repeatedly over a period of 4 weeks. During this period, the electrode maintained a calibration slope of 59 ± 3 mV/decade ($n = 10$), and the detection limit, linear range, response time, and selectivity coefficient values were almost constant. The calibration frequency over 4 weeks of continuous work under hydrodynamic conditions was also examined. The oscillations of the electrode potentials do not exceed ± 1 mV, and the slope of the calibration plot fluctuated within 0.5 mV/concentration decade. The results indicate a reasonably stable overall response of the sensor.

As the electrode characteristics under hydrodynamic flow conditions are subject to a washout effect by the carrier stream, resulting in a drifting baseline and irregularities in the response peaks, iodide samples of different concentrations were injected in random order to test the carryover effects from one sample to another. The results show that such an effect is negligible for the iodide PVC flow-through sandwich cell. However, this is not the case with a solid state iodide membrane electrode, as indicated by using a $\text{Ag}_2\text{S}/\text{AgI}$ solid state membrane electrode (Orion 94-06 A) with a flow-through cap in a cascade-flow mode.

The significant high carryover effect obtained with the solid state iodide membrane electrode limits its dynamic linear response range in FIA, lessens the repro-

TABLE 2 Potentiometric Selectivity Coefficients for Iodide-PVC Membrane Electrode

Interferent, B	$K_{i,B}^{\text{pot}}$
CH_3COO^-	7.0×10^{-4}
EDTA^{2-}	7.4×10^{-4}
HCOO^-	7.9×10^{-4}
F^-	1.0×10^{-3}
Cl^-	1.7×10^{-3}
SO_3^{2-}	2.3×10^{-3}
$\text{Fe}(\text{CN})_6^{4-}$	2.4×10^{-3}
CO_3^{2-}	2.8×10^{-3}
WO_4^{2-}	2.9×10^{-3}
PO_4^{3-}	3.4×10^{-3}
$\text{S}_2\text{O}_3^{2-}$	6.0×10^{-3}
Br^-	1.1×10^{-2}
CN^-	2.6×10^{-2}
NO_3^-	9.2×10^{-2}

ducibility for samples injected in random order, and contributes to a substantial baseline drift. A further disadvantage of the use of solid state iodide electrode is that the detection limit is given by the intrinsic solubility of the membrane material. When the electrode is exposed to a carrier solution containing no iodide, the electrode membrane undergoes a dissolution process until the solubility product of AgI has been reached. Until this steady state has been obtained, a stable potential reading cannot be taken. For this reason, carrier solutions containing iodide should be used with this type of sensor [20,23].

Effects of pH and Foreign Ions

The effect of pH of the iodide test solutions (10^{-1} to 10^{-4} M I^-) on the electrode potential was examined over the pH range 1 to 11 (not shown). The potential pH plots of the iodide sensor revealed that within this pH working range, the potentials did not vary by more than ± 1.0 mV. The performance of the iodide sensor in the presence of 16 different inorganic and organic anions was also assessed under static and hydrodynamic conditions by measuring the selectivity coefficient values ($K_{i,B}^{\text{pot}}$) using the separate solutions method [26] with a fixed concentration of the interferent (10^{-3} M). The results obtained show a reasonable selectivity for the iodide ion in the presence of many common anions (Table 2). Severe interferences are caused, however, by SCN^- and ClO_4^- . These data are similar to those obtained with the corresponding conventional coated disk membrane electrode under static conditions.

Flow-Injection Determination of Iodide and/or Iodine

The results obtained for FI potentiometric determination of 0.76 $\mu\text{g}/\text{mL}$ to 12.7 mg/mL aqueous iodide solution, each in triplicate, by sample injection in a flow stream of 5×10^{-2} M Na_2SO_4 show an average recovery of 99.4%

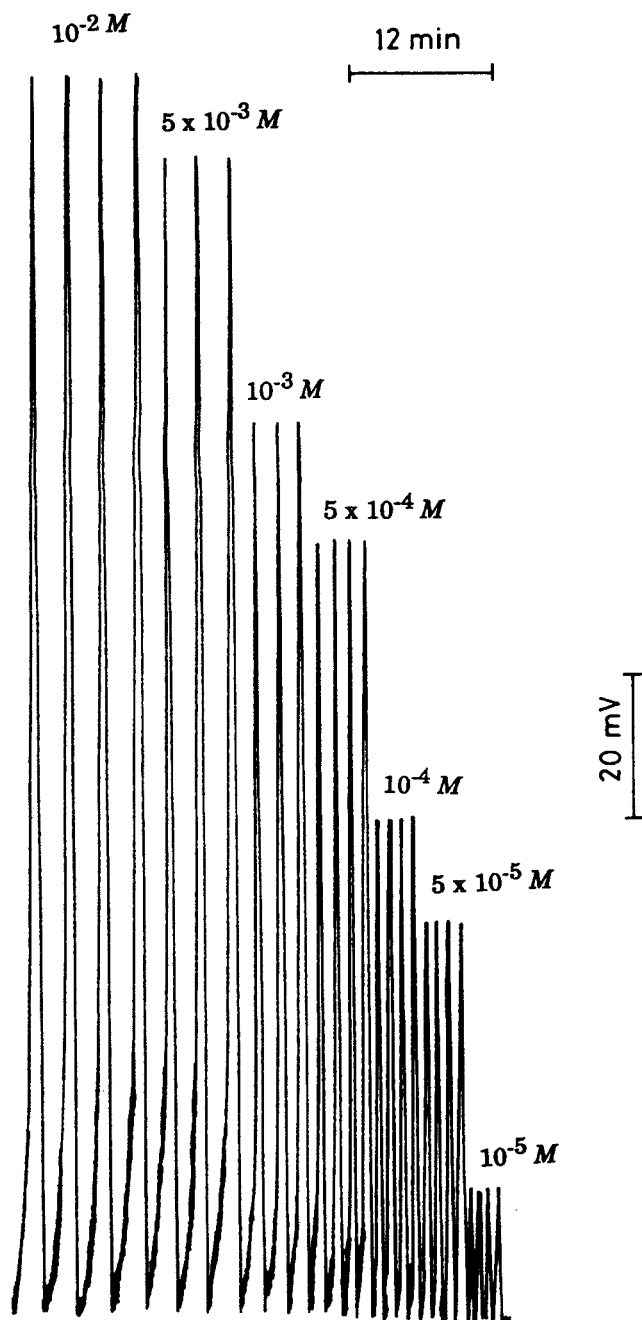


FIGURE 3. Typical FIA recorder signals produced by injection of 20 μL of standard iodide solutions in a stream of $5 \times 10^{-2} \text{ M Na}_2\text{SO}_4$.

and a mean standard deviation of 0.8%. A typical representative recorder output with a sample rate of ~ 60 samples/h is illustrated in Figure 3.

Iodine and iodide in aqueous solutions are determined by sample injection in a carrier stream of Na_2SO_4 containing a suitable reducing agent to reduce I_2 into I^- followed by monitoring the total iodide. Hydrazine sulfate, hydroxylamine hydrochloride, ascorbic acid, and sodium sulfite were tested as reductants. Whereas Na_2SO_3

affects the baseline and lowers the sensitivity, hydrazine and hydroxylamine salts require pH adjustment for optimum reduction of iodine. Furthermore, baseline noise was noticed probably due to liberation of nitrogen gas. Ascorbic acid, however, is advantageously used. It does not interfere at high concentration levels and requires no pH adjustment for instantaneous and quantitative reduction of iodine at room temperature.

A series of 20 μL standard I_2/I^- (0.5 to 500 $\mu\text{g I}_2/\text{mL}$ and 1.5 to 1500 $\mu\text{g I}^-/\text{mL}$) was injected into a carrier stream consisting of $5 \times 10^{-2} \text{ M Na}_2\text{SO}_4$ and $2 \times 10^{-2} \text{ M}$ ascorbic acid using a single-line flow-injection system. The results obtained for the total iodine and iodide show an average recovery of 99.3% and a mean standard deviation of 0.7%. These data are in good agreement with results obtained for determining iodine in the same samples by potentiometric titration with sodium thio-sulfate (redox electrode system) and measuring total iodide and iodine by a prior reduction with ascorbic acid followed by potentiometric titration with silver nitrate ($\text{Ag}_2\text{S}/\text{AgI}$ electrode system).

Sequential Flow-Injection Determination of Iodine and Iodide in Povidone Iodine

One of the possible approaches for FI determination of iodine in the presence of iodide involves a prior reduction of I_2 into I^- and measurement of the total iodide in one step, as described previously, followed by removal of iodine in a second step and measurement of the iodide content. Although removal of iodine in the presence of iodide can be carried out by solvent extraction, such a technique cannot be easily performed with a FI system. It has been reported that some aromatic compounds substituted with amino or hydroxyl groups undergo direct iodination reaction in alkaline media [28]. This allows removal of half of the iodine and permits simple FIA in homogeneous aqueous media. In this work, resorcinol was used as an iodine capture due to its high reactivity, fair solubility in aqueous media, and good solubility of its iodo derivative in the reaction medium. A preliminary study of the reaction of iodine and resorcinol by mixing different molar ratios of both reactants at ambient temperature and various pH values followed by iodimetric titration reveals that one mole of resorcinol instantaneously and quantitatively consumes 1.0 ± 0.02 mole of iodine ($n = 10$) at pH 8.5 with the formation of one mole of iodide.

Measurement of iodide in the presence of excess resorcinol was also investigated. On-line reaction of resorcinol with iodine indicates that resorcinol in basic media tends to give a negative baseline drift of the PVC iodide sensor. This is probably due to the interfering effect of resorcinol anion. In acidic media ($\text{pH} < 5$), resorcinol displays a negligible effect. Thus, the flow stream carrying the reaction products was mixed with acetate buffer of pH 4.7 before reaching the iodide detector. A mixing coil (15 cm) was inserted after the sample injection valve to ensure sample homogeneity (Figure 1).

TABLE 3 Sequential FI Determination of Povidone Iodine Using the USP and a Flow-Through Sandwich Iodide PVC Membrane Sensor

Pharmaceutical, Trade Name, and Source	Iodine (mg/mL)*		Iodide (mg/mL)*	
	USP	FIA	USP	FIA
Betadine mouth wash, 1% (w/v) (Mundipharma. AG., Switzerland)	1.17 ± 0.03	1.19 ± 0.02	1.24 ± 0.04	1.21 ± 0.03
Betadine antiseptic, 10% (w/v) (Leycol Chem. Inves., England)	8.51 ± 0.21	8.89 ± 0.05	7.24 ± 0.11	6.48 ± 0.10
Betadine vaginal douche, 10% (w/v) (Mundipharma. AG., Switzerland)	9.10 ± 0.31	8.89 ± 0.21	6.90 ± 0.21	6.73 ± 0.09
Povidone iodine, 1% (w/v) (El-Nasr Pharm. Chem., Egypt)	1.10 ± 0.02	1.12 ± 0.01	1.30 ± 0.03	1.26 ± 0.02

*Average of three measurements.

Flow-injection determination of the available I_2 and ionized I^- in povidone iodine pharmaceuticals is simply carried out by injection of the sample in a flow stream of Na_2SO_4 -ascorbic acid and measurement of the total iodide concentration equivalent to $I_2 + I^-$ (signal a). This is followed by injection of another sample in a stream of alkaline resorcinol (pH 8.5) and monitoring of the iodide concentration equivalent to $1/2 I_2 + I^-$ (signal b). Iodide and iodine concentrations are calculated from the heights of their corresponding signals. Table 3 presents results obtained for sequential FI determination of I_2 and I^- in some pharmaceuticals containing povidone iodine. The mean standard deviations for I_2 and I^- are 0.07 mg/mL and 0.06 mg/mL, respectively. The results are in good agreement with those obtained by the titrimetric methods recommended by the United States Pharmacopoeia [3]. In conclusion, the FI method described in this work for sequential potentiometric determination of iodine and iodide has several advantages. These are high reproducibility and accuracy ($\pm 0.8\%$), few manipulation steps, large sample throughput (60 S/h), and low limit of detection ($0.5 \mu g I^-/mL$).

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