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DETERMINATION OF IODIDE IN POTASSIUM IODIDE DOSAGE TABLETS USING CATHODIC STRIPPING VOLTAMMETRY WITH A CARBON PASTE ELECTRODE

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A method for the determination of iodide in potassium iodide-containing pharmaceutical formulas is presented. Special attention has been paid to the effect of thiosulphate used as the stabiliser of solid iodide. The procedure utilising a tricresyl phosphate-containing carbon paste electrode in combination with cathodic stripping voltammetry has been applied to the analysis of real samples of iodide tablets.

Introduction

Iodine as bioessential element comes into human organism through various pathways. Besides natural uptake, iodine and its compounds can be supplied from

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synthetically iodinated table salts or mineral waters [1]. Various pharmaceutical formulas containing iodide may then be another alternative source used either in medical treatments on iodine deficiency [2] or in some special applications.

The latter is the case of iodide dosage tablets [3] that are obligatorily distributed among population living near by nuclear power plants. After application, such tablets saturate the thyroid gland with iodine, thus preventing a serious damage of this organ by radioactive isotope ^{128}I released during an eventual accident of the reactor. Dosage tablets usually contain solid potassium iodide which has to be stabilised — due to oxidation — with a suitable reductant like sodium sulphite or thiosulphate [3].

Electrochemical stripping analysis with carbon paste electrodes (CPEs) has recently been shown to be a convenient analytical technique for the determination of iodide in various types of samples [4–6]. In particular, a unique tricresyl phosphate-based carbon paste (C/TCP) exhibiting considerable ion-pairing capabilities [7] has proved to be the electrode of choice for analysis of table salts and mineral waters [8-10]. The principles of the method can be summarised in the following way. Iodide (or chemically pre-reduced iodate) is accumulated at the C/TCP electrode *via* ion-pairs with protonated molecules of pasting liquid (i.e., tricresyl phosphate). This accumulation is performed at a positive potential so that the iodide moiety in the ion-associate is oxidised to the elemental iodine which is then extracted onto the carbon paste. During the subsequent stripping step, performed either as cathodic voltammetric scan [7–9] or with the aid of negative constant current in the stripping potentiometric mode [10], re-extraction of reduced iodine takes place, thus giving rise to the corresponding analytical signal.

Applications of the C/TCP electrode described above can be characterised as those belonging to trace analysis because the samples of salts or mineral waters contain iodine at the low ppm level. In this article, it is shown that stripping voltammetric method based on the C/TCP electrode can also be used for analysis of iodide-containing dosage tablets that represent typical samples with a higher concentration level of iodide (about 10% potassium iodide per tablet [3]).

Experimental

Apparatus and Electrode System

A polarographic analyzer (Model PAR 174, Princeton Applied Research, U.S.A.) was used coupled with a personal computer *via* an interface card (PC AD/DA-14, Model FPC-011; Flytech Technology, U.S.A.). This assembly controlled *via* an "ADDA-174 A" software [9] was connected with an SMDE electrode stand (Laboratorní přístroje Praha, Czech Republic) adapted for measurements with CPEs.

The working electrode was a CPE based on tricresyl phosphate-containing carbon paste ("C/TCP" [7]) . The paste consisting of 0.5 g spectroscopic graphite powder ("RW-B", Ringsdorff Werke, Germany) and 0.3 ml tricresyl phosphate (mixture of isomers, Fluka) was homogenised using a pestle and mortar. The prepared paste was then packed into electrode holder equipped with a piston [11]. A Ag/AgCl electrode (containing 1 M KCl as the inner electrolyte) served as the reference whereas self-made platinum plate represented the counter electrode.

Stirring was performed with a Teflon®-coated magnetic bar at approx. 600 rpm. The pH was measured using a digital pH meter (Model 420A, Orion, USA) equipped with a combined glass pH sensor (Model OP-0808P, Radelkis, Hungary).

Chemicals and Reagents

All chemicals and standard solutions used were of analytical reagent grade and purchased from Lachema Brno (Czech Republic) except for sodium chloride (Suprapur® purity, Merck). For the preparation of supporting electrolytes and sample solutions, 1 M stock solutions of NaCl, HCl, and HNO_3 were made. The standard of potassium iodide was prepared as 0.01 M KI and its diluted solutions (< 0.001 mol l^{-1}) were made fresh daily. For some testing measurements, the solutions of 0.01 M Na_2SO_3, 0.01 M $KMnO_4$, and 0.01 M $K_2Cr_2O_7$ were also used.

Water used throughout the experimental work was obtained by passing deionised water through a laboratory-made distillation unit. All solutions to be analysed were purged with argon gas (purity 99.996%, Linde Technoplyn).

Samples

Potassium iodide-containing dosage tablets were obtained from a company responsible for their distribution in the area of Dukovany nuclear power plant (South Moravia, Czech Republic). This product of a commonly marketed pharmaceutical contained a package of four yellowish pills with a microcrystalline cellulose matrix.

The content of the active component in the tablets weighing each about 0.6 g was declared as 65 mg KI. As a stabiliser, sodium thiosulphate, $Na_2S_2O_3$, was added, but its amount was not specified.

Solutions for Analysis

Model Solutions. Unless stated otherwise, model and test solutions were prepared fresh before use. Specification of their composition is given later — correspondingly in the text. Some of test solutions containing a spike of HNO_3 as oxidising agent were pre-heated for 5 min at approx. 70 °C in ordinary water bath and cooled down before use.

Sample Solutions. A stock sample solution was prepared as follows: The whole tablet was intimately ground in a mortar, finely powdered, transferred quantitatively to a volumetric flask, acidified with 1 ml 65 % HNO_3, and diluted with water to the desired volume. In this way, two stock solutions made of two different tablets from the same packaging were prepared. Prior to determinations, both stock sample solutions (SSS) were diluted with distilled water, usually at a ratio of 1:10.

The sample solutions proper were prepared by adding 2 ml SSS (diluted) to a mixture of 14 ml H_2O + 2 ml 1 M NaCl + 2 ml 1 M HNO_3 (pre-heated at ca 70 °C). After purging with argon for 5 min, the sample solutions were taken for voltammetric analysis (see below) without any other pretreatment.

Procedures

Renewal of the C/TCP Electrode. Approx. 2 mm carbon paste was extruded from the electrode holder, cut off, and the surface was smoothed with a wet filter paper. Such carbon paste regeneration was made before each next measurement.

Stripping Voltammetry. In the supporting electrolyte containing diluted stock sample solution, the accumulation (preconcentration) was performed at +0.7 V vs Ag/AgCl (typically for 30 s), and after the rest period (15 s), the proper voltammetric measurement was performed from +0.7 to −0.3 V in the cathodic direction at a scan rate of 20 mV s^{-1}, using the pulse height of −50 mV, and the sampling rate of 5 data s^{-1}.

Reference Titrimetric Determination

An official titration method by ČSN [12] selected for the reference determination was based on chemical oxidation of iodide in the sample solution with hypochlorite whose excess could be removed by a short boiling the sample with formic acid

$$3\ CaCl(ClO) + I^- \rightarrow 3\ CaCl_2 + IO_3^- \quad (1)$$

$$CaOCl_2 + HCOOH \rightarrow CaCl_2 + CO_2 + H_2O \quad (2)$$

Afterwards, a solution of iodide was added to the sample with the iodate formed, and an equivalent amount of the iodine released was subsequently titrated using a solution of thiosulphate standardised against dichromate. The method utilised a classical indication of the titration end-point with a starch solution.

Data Processing and Evaluation

In order to quantify the concentration, the standard addition method with at least two aliquots was used. The analytical signals were computed as peak areas [8–10] and the results of determinations calculated by means of a statistical method recommended for small sets of experimental data [13].

Results and Discussion

Choice of Experimental Conditions and Parameters

Practically all the conditions such as the choice of the carbon paste and its regenerating, the selection of the main components of the supporting electrolyte and of the individual instrumental parameters could be used accordingly to the previous procedure for the determination of iodide in table salts [8,9].

Also in this method, the samples had always to be deaerated with an inert gas to remove air oxygen dissolved in the solutions and interfering with measurements carried out in the cathodic scan direction [7].

Studies on the Effect of Thiosulphate upon the Response of Iodide

In contrast to table salts, the samples of iodide-containing pharmaceuticals contained $Na_2S_2O_3$ which, as a generally reactive agent, could affect even highly selective measurement based on the C/TCP electrode [8–10]. Thus, the effect of the $S_2O_3^{2-}$ ions on the response of reduced iodine was investigated using specially proposed testing measurements.

As test substances for decomposing thiosulphate, $KMnO_4$, $K_2Cr_2O_7$, and HNO_3 were studied on model samples. Although permanganate as well as dichromate had been found to be effective to oxidise the $S_2O_3^{2-}$ ions, both were inapplicable. The reason was that MnO_4^- and $Cr_2O_7^{2-}$ ions themselves gave rise

to a signal overlapping the response of interest. This has confirmed the previous observation [5] that such anions are capable of forming the corresponding ion-pairs whose cathodic reduction may then compete with that of iodine. In this respect, nitric acid was shown much more convenient since neither nitrate nor its reaction products exhibited any ion-pairing affinity towards the C/TCP electrode. Nitric acid was therefore taken as the oxidant of choice

$$2\,HNO_3 + 3\,S_2O_3^{2-} \rightarrow 3\,SO_4^{2-} + 3\,S + 2\,NO + H_2O \qquad (3)$$

Figure 1 depicts typical responses of reduced iodine in the presence of nearly equal concentration of thiosulphate in the supporting electrolyte. When comparing the sets of voltammograms in A and B, it is evident that oxidation of the $S_2O_3^{2-}$ ions with HNO_3 was effective solely in pre-heated solutions.

Recovery rate determinations in model solutions with I^- and $S_2O_3^{2-}$ ions in a ratio of 1:2 and 1:5 revealed that the oxidation performed at ambient temperature had proceeded incompletely with a yield of 25 – 50 %. The recovery for analysis of solutions with identical composition and oxidised at ca 70 °C was then satisfactory when varying within 85 – 100 %. The latter results also proved that nitric acid or its reaction products had no effect on the proper measurement and the signal of interest.

Rather atypical shape of the responses of reduced iodine has already been reported in the original reports [8,9]. A considerable width of the signals is a consequence of the extractive entrapment of accumulated species and their subsequent re-diffusion during voltammetric reduction [9]. At higher concentrations of iodide, the responses typically exhibited several maximums. Their existence can be attributed to a synergistic reduction when besides iodide alone also various iodide aggregates like I_3^-, I_5^- or I_2Cl^- are formed during the accumulation process in salinic supporting medium (see legend). Since such species exhibit somewhat different values of the standard redox potential, $E^0_{(Ox/Red)}$, compared to that of I^- alone (see [14]), it seems logical that even their reduction peak potentials, E_P, may slightly differ from each other when one considers a direct relation between both $E^0_{(Ox/Red)}$ and E_P [15]. With respect to evaluating such complex responses, it should be emphasised that the above-mentioned aggregates always are electrochemically transformed to elementary iodine

$$2\,I_3^- \rightarrow 3\,I_2^0 + 2\,e^- \qquad (4)$$

$$2\,I_5^- \rightarrow 5\,I_2^0 + 2\,e^- \qquad (5)$$

$$I_2Cl^- \rightarrow I_2^0 + Cl^- \qquad (6)$$

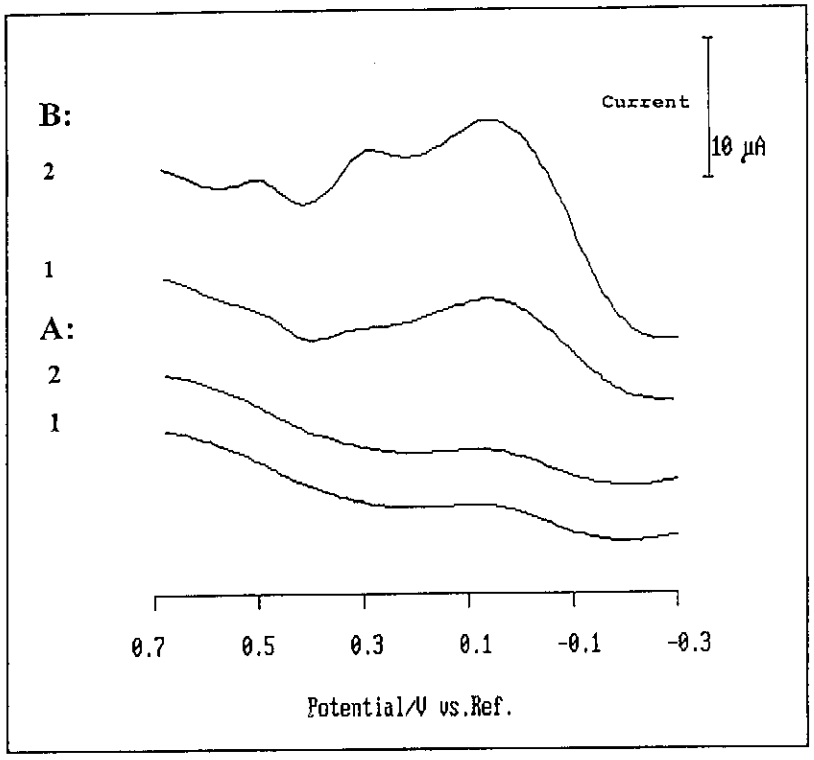

Fig. 1 Effect of the reduction of thiosulphate with nitric acid upon the response of reduced iodine A: model solution oxidised with HNO_3 at 20 °C, B: model solution pre-heated at 70 °C for 5 min. 1) model solution + 5×10^{-5} M KI, 2) model solution + 1×10^{-4} M KI. Experimental conditions: differential pulse cathodic stripping voltammetry (DPCSV); tricresyl phosphate-based carbon paste electrode (C/TCP); model solution: 0.1M NaCl + 0.1M HCl + 0.1 M HNO_3 + 1×10^{-4} M $Na_2S_2O_3$; accumulation time, t_{ACC} = 30 s; the rest (equilibrium) period, t_R = 15 s; accumulation potential, E_{ACC} = +0.7 V vs Ag/AgCl; final potential, E_{FIN} = −0.3 V; scan rate, r = 20 mV s^{-1}; pulse height, ΔE = −50 mV; purging: 5 min. with Ar.

i.e., identically as iodide itself. Thus, the resultant concentration of iodide can be ascertained from the peak area comprising all the individual peaks [9,10].

The voltammograms in Fig. 2 demonstrate the disastrous effect of the $S_2O_3^{2-}$ ions present in the solution at a higher concentration excess with respect to I^- ions (10 : 1 and more). As seen, there is actually no signal for the reduction of iodine showing that the destruction of thiosulphate with HNO_3 has been ineffective. Apparently, the disappearance of iodine was due to its reaction with the $S_2O_3^{2-}$ ions that remained non-decomposed in the mixture. Thiosulphate alone or its reaction products — including dispersed sulphur — had again no influence

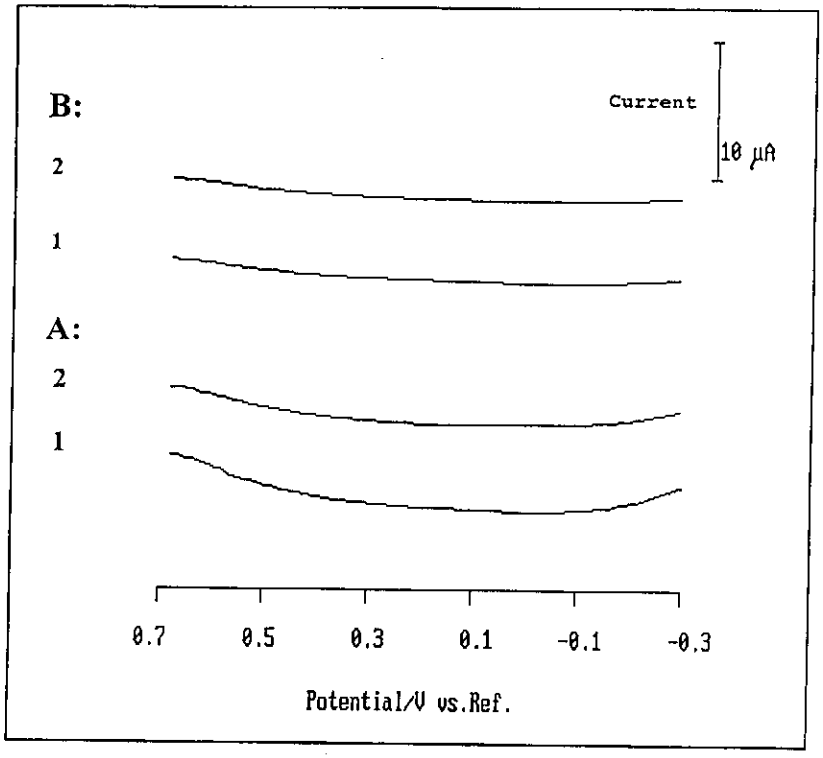

Fig. 2 Effect of higher concentrations of thiosulphate upon the response of reduced iodine A: unheated model solution, B: pre-heated model solution. 1) model solution + 5×10^{-5} M KI, 2) model solution + 1×10^{-4} M KI. Experimental conditions: model solution: 0.1 M NaCl + 0.1M HCl + 0.1 M HNO_3 + 1×10^{-3} M $Na_2S_2O_3$. For other parameters, see caption in Fig. 1.

on the base-line of the C/TCP electrode, which was confirmed by means of comparative measurements in the blank electrolytes (i.e., without I^- ions).

Analysis of Samples

The investigations discussed in the previous paragraph have implied that a negative effect of thiosulphate in the sample can effectively be suppressed to a certain extent and a ca 10-fold excess of $S_2O_3^{2-}$ over I^- ions already makes the determination of iodide impossible. Regarding iodide-containing tablets, their declared composition, and the amount of potassium iodide in relation to the overall weight of one pill, it was apparent that the content of thiosulphate — although unspecified — could not reach a level in which this constituent would seriously

interfere with the determination of iodide.

In Table I, the results of analysis of both samples are summarised together with those obtained with the reference titrations [12]. The quite good agreement between both methods confirms that the results have not been affected significantly by the presence of thiosulphate. By the way, its presence in the solutions did not permit a simpler titration utilising oxidation of iodide in the samples with dichromate. Some preliminary tests clearly showed that this procedure did not provide a well-defined end-point. Due to this, the method based on strongly oxidative hypochlorite and involving the intermediate step $I^- \rightarrow IO_3^-$ was found to be absolutely necessary.

Table I Analysis of iodide-containing dosage tablets.

Sample (tablet)	Results of determinations, mg KI per pill[a] (number of analyses)			
	Stripping voltammetry with C/TCP electrode		Reference titration [12]	
No. 1[b]	48.3	(1)	-	
No. 1[c]	52.4 ± 5.8	(4)	54.4 ± 8.3	(2)
No. 2[c]	69.3 ± 4.0[d]	(4)	65.7 ± 5.1	(2)

Legend: [a]given as intervals $\bar{x} \pm k_M R$ where $\bar{x}$ is the arithmetic mean, R denotes the spread between the individual measurements, and k_M is a statistical criterion (for details, see [14]); [b]undiluted stock sample solution, [c]diluted 1 : 10; [d]calculated from three analyses only, one determination provided the result which had to be eliminated as an outlying value

Somewhat lower content of iodide ascertained in tablet No. 1 (below the declared value, i.e., << 65 mg KI) may indicate that a part of the active substance could be lost during the storage of the product despite the stabiliser used. This assumption is also supported by the appearance of the tablets having a typical yellowish colour. Instability of solid potassium iodide is known and, among others, it has stimulated a new trend in the iodination of table salts by using more stable potassium iodate [1].

Figure 3 illustrates the voltammograms obtained by analysing the sample solution of tablet No. 1. The curves again manifest a characteristic broadness of the signal and its splitting. Dashed lines in the figure then indicate a manner in which the areas of the individual responses can be evaluated.

It is worth mentioning that the method utilising the C/TCP electrode could also be used to analyse directly undiluted stock sample solution. This represents rather atypical application if one considers that stripping voltammetry is typically employed for the quantification of analytes at the trace or even ultratrace level [15].

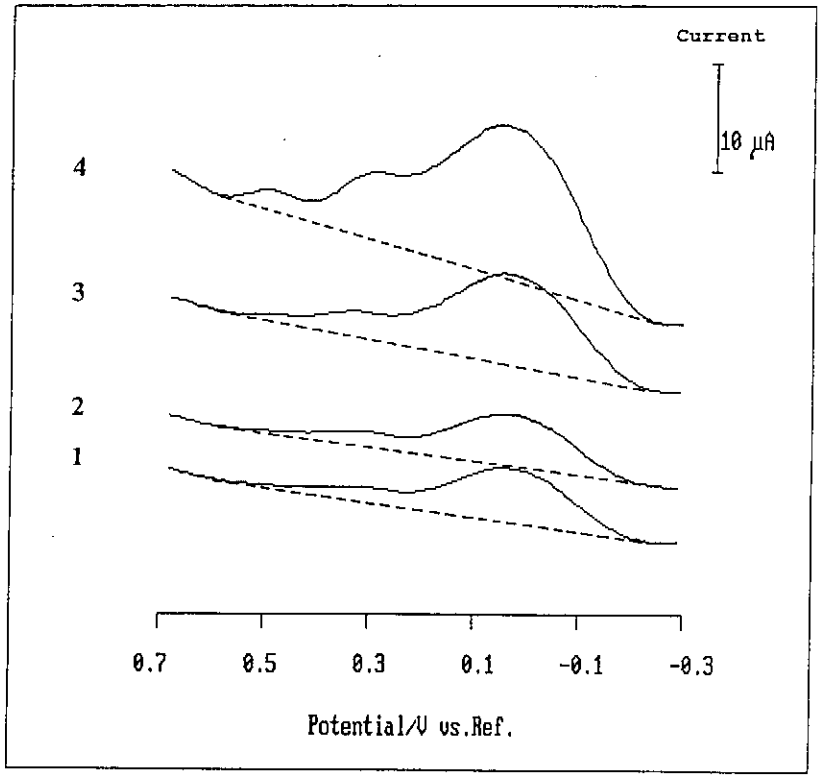

Fig. 3 Typical voltammograms obtained by analysing iodide-containing dosage tablets.1) sample, 2) replicate; 3) 1st, 4) 2nd standard addition. Experimental conditions: DPCSV; C/TCP; sample: tablet No.1; sample solution (pre-heated at 70 °C): 2 ml SSS (1 : 10) + 2 ml 1M NaCl + 2 ml 1M HNO_3 + 14 ml H_2O; standard addition aliquots of 50 µl 0.01 M KI. For other parameters, see caption in Fig. 1

It can be concluded that voltammetric method proposed herein for analysis of iodide-containing dosage tablets offers an interesting alternative to traditional titrations that are usually the methods of choice for analysing samples with a higher content of iodide. Compared to these traditional titrimetric procedures, the method with the C/TCP electrode is simpler, less time-consuming, more economical (when sparing chemicals), and does not require the use of aggressive oxidants with active halogen.

Acknowledgements

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