

Automatic titrimetric determination of iodide in some pharmaceutical contrasting preparations

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Abstract: Automatic titrimetric methods with catalytic, spectrophotometric and potentiometric monitoring of the course of titration were applied for determination of iodide content in iopanoic acid, 2-(3-amino-2,4,6-tri-iodobenzyl)butyric acid, as well as in the mixture of sodium amidotrizoate (sodium 3,5-diacetamido-2,4,6-tri-iodobenzoate), and meglumine amidotrizoate (*N*-methylglucamine salt of 3,5-diacetamido-2,4,6-tri-iodobenzoic acid), in some pharmaceutical contrasting preparations. After combustion of the sample in an oxygen atmosphere and absorption of products in hydrazine sulphate solution, the iodide present was titrated with a standard solution of silver nitrate. In catalytic titrations, the system persulphate-sulphanilic acid (acetate buffer pH 4.35) in the presence of 2,2'-bipyridine as an activator served as the indicator reaction. The results obtained were compared with those of the official methods. Amounts of iodide of about 1.2 mg per aliquot of analyte were determined with a standard deviation less than 1.9%.

Keywords: *Catalytic spectrophotometric titrations; iodide determination; pharmaceutical contrasting preparations; computer-controlled titrations.*

Introduction

Iopanoic acid, 2-(3-amino-2,4,6-tri-iodobenzyl)butyric acid, is commonly used in medicine as an X-ray cholecystographic agent, whereas a mixture of sodium amidotrizoate (sodium 3,5-diacetamido-2,4,6-tri-iodobenzoate), and meglumine amidotrizoate (*N*-methylglucamine salt of 3,5-diacetamido-2,4,6-tri-iodobenzoic acid), serves as an X-ray urographic contrasting preparation.

For determination of these preparations, the Farmakopeja SFRJ [1] recommends an argentometric determination of iodide content after a prolonged sample decomposition. This operation is carried out by refluxing the analyte with a solution of sodium hydroxide in the presence of zinc and the reaction mixture is filtered through a glass filter crucible. The clear filtrate is used for the analysis. According to the British Pharmacopoeia [2], iopanoic acid and sodium amidotrizoate are determined by iodometric titration after liberation of iodine from the preparation in a way similar to that already described. On the other hand, the US Pharmacopoeia [3] recommends determination of iopanoic acid by a neutralization titration after appropriate multiple extraction, first with hexane and then with ethanol.

In view of the fact that catalytic spectrophotometric titrations have been successfully applied for determination of iodide in model solutions [4], the aim of the present work was to investigate the possibility of their application for determination of iodide content in Holevid tablets and Urotrast ampoules, containing iopanoic acid and a mixture of sodium amidotrizoate and meglumine amidotrizoate, respectively, as active component.

In addition, an automatic potentiometric titration procedure was applied, using a silver wire as indicator electrode.

The procedures developed were also applied to the determination of inorganic iodide in the above preparations, present as a synthetic impurity.

Experimental

Reagents and samples

All chemicals used were of analytical reagent grade. Solutions were prepared with doubly-distilled water.

Contents of iodide were determined in the following pharmaceutical preparations: Holevid tablets (500 mg iopanoic acid tablet⁻¹) and Urotrast 75% ampoules (370 mg iodide ml⁻¹) (Krka, Novo Mesto, Slovenia).

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Standard silver nitrate solution (5.0 mM) was tested against a standard solution of potassium iodide by all the methods applied in the present investigations.

Solution of potassium persulphate in acetate-buffer pH 4.35 (0.06 M), sulphanilic acid (0.07 M), 2,2'-bipyridine (0.048 M) as well as the acetate buffer pH 4.35 were prepared as described previously [4]. A saturated solution of hydrazine sulphate was employed.

Apparatus

The course of automatic catalytic spectrophotometric titrations was monitored on a Carl Zeiss spectrophotometer at 535 nm, with a Ti accessory for titrations.

The automatic potentiometric titrations were performed with the aid of a silver electrode connected via a suitable salt bridge to a Radiometer saturated calomel electrode, and the appropriate resistor to ensure a zero-current regime.

In all cases, the automation of the procedure was realized by connecting the titration system to an Aston 110 XT personal computer via a laboratory-made measurement-control unit.

The titrant was added continuously from a Radiometer ABU 12 automatic piston burette at an optimum rate of $0.710 \text{ ml min}^{-1}$.

Procedure

Sample preparation for inorganic iodide determination. An amount of ground Holevid tablets containing about 1.6 g of iopanoic acid was dissolved in a 25 ml flask and filled to the mark with water. For the spectrophotometric titrations, a portion of the solution was transferred to a 10 ml centrifuge tube, centrifuged for about 10 min, and the supernatant used for determination.

The content of one Urotrast 75% ampoule was diluted with water in a 100 ml flask and filled to the mark.

Sample preparation for determination of total iodide content. A weighed sample of ground Holevid tablets containing about 9 mg of iopanoic acid was burnt in an oxygen atmosphere in a combustion flask by Schöniger's method [5]. The combustion products were absorbed in 10 ml hydrazine sulphate solution; the solution obtained was transferred to a 50 ml flask and filled to the mark with water.

To analyse Urotrast 75% ampoules, an amount of the solution containing about 40 mg of the mixture of meglumine amidotrizoate and sodium amidotrizoate was weighed, and treated as described above. The solution obtained was adjusted to 100 ml with water.

Blank solutions were prepared in the same way as the sample solutions.

Measurements

Catalytic spectrophotometric titrations. To 10.00 ml of the solution prepared for analysis were added the following solutions: 10.00 ml potassium persulphate, 1.00 ml sulphanilic acid, and 1.00 ml 2,2'-bipyridine. The mixture was titrated with the standard silver nitrate solution.

Potentiometric titrations. To 10.00 ml of the solution, 10.00 ml of buffer pH 4.35 was added, and the mixture titrated with the standard silver nitrate solution. The end-point was determined using a computer program for finding the intersection of the straight lines before and after the equivalence point, or, from the maximum of the derivative titration curve. Results were corrected for the blank titration. Procedures used in comparative determinations were as described in the Farmakopeja SFRJ [1].

Results and Discussion

In the catalytic titrations, a solution of iodide is titrated with a solution of silver nitrate in the presence of components of the indicator reaction persulphate-sulphanilic acid (in acetate buffer pH 4.35). In parallel to the main reaction of iodide and silver ion, proceeds the reaction of oxidation of sulphanilic acid by persulphate, which is catalysed by Ag(I). In order to accelerate this reaction it is necessary to add 2,2'-bipyridine as an activator.

The optimal experimental conditions in respect of the indicator reaction components, as well as the rate of the titrant addition in the iodide determination were as established in previous work [4].

Two different solutions for the absorption of the products of sample oxidation were employed. When a solution of hydrogen peroxide in the presence of magnesium was used [6], the resultant catalytic spectrophotometric titration curves were of a shape unsuitable for end-point determination. However, use of hydrazine

Table 1

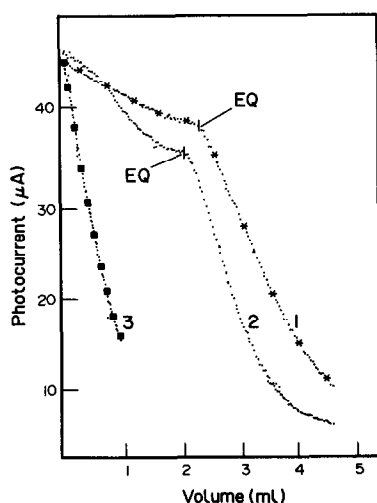
Results of determination of iopanoic acid and mixture of sodium amidotrizoate and meglumine amidotrizoate in pharmaceutical preparations (six titrations in each case)

Method	Pharmaceutical preparation			
	Holevid tablets (500 mg iopanoic acid per tablet)		Urotrast 75% ampoules (370 mg I ⁻ per ml)	
	Found*	RSD	Found†	RSD
Catalytic spectrophotometric titration	488	1.0	371	1.9
Potentiometric [Ag/SCE] titration	484	1.7	368	0.5
Official method [1]	497	0.8	367	0.6
<i>F</i> -ratio‡		7.46		1.14

* Found, mg iopanoic acid per tablet.

† Found, mg I⁻ per ml.

‡ The theoretical values are: 3.68 ($P = 0.05$) and 6.36 ($P = 0.01$) for $f_1 = 2$ and $f_2 = 15$.

**Figure 1**

Automatic catalytic spectrophotometric titration curves for 1.2 mg of iodide in Urotrast 75% ampoules (1), Holevid tablets (2), and the blank (3) with 5.0 mM silver nitrate solution. EQ = Equivalence point.

sulphate solution resulted in titration curves of satisfactory shape.

Figure 1 shows typical titration curves for iodide determination in Urotrast 75% ampoules (curve 1), and Holevid tablets (curve 2). In both cases the titration curves are suitable for end-point determination.

Some of the results obtained are presented in Table 1. According to one-way analysis of variance in the case of Urotrast 75% ampoules, there are no significant differences in respect of accuracy between the three methods, whereas precision of the catalytic spectrophotometric method is the lowest of the three.

Analysis of the results of iopanoic acid determinations in Holevid tablets showed no

significant difference in respect of the method precision. The results of spectrophotometric and potentiometric titrations are in good agreement [$t = 1.01$ for $f = 10$, theoretical value is 2.23 ($P = 0.05$)]. The results obtained by the official method are somewhat higher if compared to those of catalytic spectrophotometric and potentiometric titrations [$t = 3.47$ and 3.53, respectively, for $f = 10$]. However, all the results obtained agreed well with the declared content of the active substance.

Inorganic iodide contents in the investigated pharmaceutical preparations were also determined by the same procedure. The spectrophotometric titration gave 0.934 mg I⁻ per ampoule in the case of Urotrast, whereas in the case of Holevid tablets the iodide content was below the determination limit. Similar results were obtained by potentiometric titrations (Urotrast 75% ampoules 0.938 mg per ampoule, Holevid preparation below the determination limit).

From the above results it may be concluded that the automatic titrimetric procedures applied in the present work are simpler, faster, and less expensive than the official methods for determination of iodide content in the given pharmaceutical preparations.

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