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Short Communication

Coulometric determination of sulphisomidine, sulphamethoxydiazine and sulphamoxole

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Introduction

Sulphamidine preparations belong to the large group of chemotherapeutica, i.e. antibacterial agents. Their action may be bacteriostatic or bactericidal depending on the mechanism of action of the microorganism. Sulphisomidine belongs to the group of pyrimidine sulphonamides and is officially used by the French, German and Japanese Pharmacopoeias. A new method for the assay of sulphisomidine comprises its potentiometric titration with copper(II) sulphate or silver nitrate by using a corresponding ion-selective electrode [1]. Sulphamethoxydiazine belongs to the group of sulphonamides with prolonged action and is officially used by the British, Czech and Romanian Pharmacopoeias [2]. Sulphamoxole is quantitatively analysed fluorometrically [3] and by IR spectroscopy [4].

With the aim of developing a common method for the determination of small quantities of the aforementioned sulphonamide preparations we attempted to establish conditions for the application of the coulometric method.

Experimental

Reagents and materials

Sulphisomidine and Didrosulfon drops were produced by Zdravlje (Leskovac, Yugoslavia); sulphamethoxydiazine and Fortesul tablets by Pliva (Zagreb); and sulphamoxole and Supristol tablets by Krka (Novo Mesto, Yugoslavia).

Apparatus

The apparatus used is described in our previous paper [5].

Standard and sample preparation

A stock solution of sulphisomidine contained 25 mg of sulphisomidine in 100 ml of water. The stock solution for the analysis of Didrosulfon drops was of the same concentration.

The stock solution of sulphamethoxydiazine contained 20 mg of this substance in 100 ml of methanol. The stock solution for the analysis of sulphamethoxydiazine in Fortesul tablets was made as follows: 10 tablets were weighed, pulverized and a portion of the powder containing nominally 20 mg of sulphamethoxydiazine was weighed, treated with 90 ml of methanol, filtered off and the filtrate was made up to 100 ml with methanol.

The stock solution of sulphamoxole contained 20 mg of this substance in 100 ml of methanol. For the determination of the content of sulphamoxole in Supristol tablets, 10 tablets were weighed, pulverized and a portion containing nominally 20 mg of sulphamoxole was weighed, treated with 90 ml of methanol with stirring, filtered off and the filtrate was made up to 100 ml with methanol.

The indicator solution contained 20 mg of Methyl Orange in 100 ml of water.

The supporting electrolyte comprised 0.1 M sulphuric acid and 2 M sodium chloride.

All solutions were made immediately prior to use and all chemicals used were of analytical reagent grade.

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Procedure

In the anode compartment of the apparatus for the coulometric titration were placed: 40 ml of the supporting electrolyte, 0.1 ml of the indicator solution and aliquots of the stock solution of sulphisomidine, sulphamethoxydiazine and sulphamoxole, respectively. A constant current of 1 mA was passed through the solution until the red colour of the indicator was bleached. The time of the titrant generation was measured with a chronometer and a blank was run in parallel. The difference between the number of coulombs used in the titration of the solution being analysed and the blank gives the number of coulombs for the titration of the investigated substance. The amount of substance is calculated using Faraday's laws. One coulomb corresponds to 1.4421 mg of sulphisomidine, 0.7262 mg of sulphamethoxydiazine and 0.4616 mg of sulphamoxole, respectively.

Results and Discussion

The chemical properties of these compounds indicate the possibility of their reaction with halogens [6, 7] and therefore the investigation was directed towards the establishment of the optimum electroanalytical conditions for an accurate and reproducible determination of these sulphonamides.

Investigations of the electrochemical reactions for chlorine electrogeneration in the presence of the investigated sulphonamides have shown that their presence does not interfere with concurrent reactions for electrogeneration, providing the supporting electrolyte contains 0.1 M sulphuric acid and 2 M sodium chloride. Under these reaction conditions sulphisomidine reacts with electrogenerated chlorine in a 1:1 molar stoichiometric ratio, whereas in the case of sulphamethoxydiazine this ratio is 1:2, and in the case of sulphamoxole is 1:3.

The composition of the supporting electrolyte used is of great importance on account of unfavourable concurrent reactions which may occur and interfere with the electrogeneration of chlorine by reducing the 100% current efficiency in chlorine generation. Thus, if the concentrations of hydrogen and chloride ions in the supporting electrolyte are too high, oxidation of the platinum anode may occur, whereas if the concentration of chloride ions is small, water may be oxidized at the anode which also decreases the efficiency of chlorine electrogeneration.

According to data reported in the literature, the chlorination reaction is much faster than that of bromination (approx. 50 times) [8], so stronger currents could be applied; by this method the rate of sulphonamide determination was more efficiently achieved and the change of the indicator colour could be clearly observed, which enabled accurate detection of the titration end point. Due to a higher rate of determination the coulometric analysis was carried out chlorimetrically. Methyl Orange was used as an indicator because the rate of its reaction with chlorine is slower than the chlorination reaction of the investigated sulphonamides.

Since the aforementioned sulphonamides were also assayed in various pharmaceutical formulations, we have investigated the effect of the usual excipients and ingredients on the electrogeneration of chlorine and their concurrence in the reaction of this halogen with the investigated sulphonamides. It has been found that the presence of excipients such as starch, talc or magnesium stearate and in-

Table 1
Results of the coulometric titration

Taken (mg)	Found (mg)	Found (mg)
	Sulphisomidine	
	Pure substance	Didrosulphon drops
0.025	0.025 ± 0.001*	0.025 ± 0.001*
0.100	0.099 ± 0.001	0.102 ± 0.001
0.175	0.175 ± 0.001	0.175 ± 0.001
0.250	0.249 ± 0.002	0.250 ± 0.001
0.375	0.375 ± 0.001	0.374 ± 0.001
0.500	0.496 ± 0.001	0.501 ± 0.001
	Sulphamethoxydiazine	
	Pure substance	Fortesul tablets
0.020	0.023 ± 0.001*	0.019 ± 0.001*
0.040	0.040 ± 0.001	0.040 ± 0.001
0.060	0.060 ± 0.001	0.060 ± 0.001
0.080	0.080 ± 0.001	0.080 ± 0.001
0.100	0.098 ± 0.001	0.102 ± 0.001
0.120	0.116 ± 0.001	0.119 ± 0.001
	Sulphamoxole	
	Pure substance	Supristol tablets
0.020	0.021 ± 0.001*	0.021 ± 0.001*
0.040	0.040 ± 0.001	0.040 ± 0.001
0.060	0.060 ± 0.001	0.060 ± 0.001
0.080	0.080 ± 0.001	0.080 ± 0.001
0.100	0.102 ± 0.001	0.100 ± 0.001
0.140	0.140 ± 0.001	0.140 ± 0.001
0.160	0.157 ± 0.001	0.159 ± 0.001

*Standard deviation (n = 7).

gredients such as sucrose and lactose does not affect the accuracy of the determination. Therefore this method could be directly applied to the assay of the sulphamethoxydiazine content in Fortesul tablets as well as the sulphamoxole content in Supristol tablets, whereby the presence of trimetoprime did not interfere with the process of the quantitative analysis. Direct coulometric determination of the sulphisomidine content in Didrosulfon drops could also be performed since the presence of dihydrostreptomycin did not affect the course of the reaction. The results of the determination of the investigated sulphonamides in the pure state and in pharmaceutical formulations are presented in Table 1.

From the results obtained it can be concluded that the developed method is accurate and reproduciblie and can be applied to the assay of investigated compounds in various pharmaceutical formulations.

In comparison with other methods prescribed by different pharmacopoeias the procedures of which require amounts of compound up to 500 mg for analysis, the chlorocoulometric method is advantageous since it can be carried out with very small quantities of investigated sulphonamides. Due to its simplicity, accuracy and reproducibility, the developed method can be recommended for the routine analysis of the investigated compounds.

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