Acta Poloniae Pharmaceutica – Drug Research, Vol. 59 No. 3 pp. 169–170, 2002

ISSN 0001-6837
Polish Pharmaceutical Society

ACIDIMETRIC TITRATION OF MEDICINES BEING SALTS OF WEAK ACIDS AND DETERMINING THE END–POINT BASED ON THE IODATE(V)–IODIDE REACTION

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Abstract: A sample being a salt of weak acid in a solvent is determined with hydrochloric acid in the presence of iodate, iodide and starch. The excess acid colours the solution blue.

Keywords: drug analysis, phenobarbitalum–Na, cyclobarbitalum–Ca, sulfacetamidum–Na, acidimetry, iodate–iodide reaction

The iodate(V)–iodide reaction proceeded in acidic medicum is used for various purposes due to quantitative dependence of the amount of generated iodine on the amount of iodate(V) at excess of acid and iodide, or the amount of acid at excess of iodate(V) and iodide (1).

The reaction is also used to establish the end–point for weak bases (atropine). In this paper this method is used for titration of drugs being salts of weak acids. The titration is carried out on a sample in a solvent in the presence of iodate, iodide and starch. An excess of acid colours the solution blue.

EXPERIMENTAL

Preparations under examination:

Phenobarbitalum natrium – a powder manufactured by GALENUS in Warsaw, batch no. 38690698; Cyclobarbitalum calcium – tablets manufactured by POLFA S.A. at Tarchomin, batch no. 11198; Sulfacetamidum – eye drops manufactured by POLPHARMA S.A. in Starogard Gdański, batch no. 80700.

Reagents and solutions:

Sodium nitrate (III) – 0.1 mole/l standard solution; potassium bromate (V) – 0.0167 mole/l standard solution; potassium bromide; anhydrous ethanol; diethyl ether; potassium iodate (V) – 0.4% solution; potassium iodide – 1.4% and 10% solutions; acetic acid – 80% and 8.33% solutions; hydrochloric acid – 10% solution and 10^{-2} mole/l standard solution; starch – 1% solution; sodium thiosulphate (VI) – 0.1 mole/l standard solution.

The reagents were manufactured by POCh in Gliwice.

Titration procedure

The sample sizes:

- Phenobarbitalum natrium – weighed amounts of approx. 0.02 g of preparation;
- Cyclobarbitalum calcium – weighed amounts of approx. 0.03 g of ground tablets;
- Sulfacetamidum natrium – the content of ampoule was dissolved in water (1:10) and volume of the solution taken for titration was 2.0 ml.

Establishing the titrant in blank test

1 ml of iodate(V), starch solution and 10 ml of iodide solution were added to 100 ml of water and determined with hydrochloric acid at concentration of 10^{-2} mole/l until the first navy blue tint was reached (colour intensity increased gradually) with drops added approximately at 5 second intervals. At that phase the solution was agitated vigorously.

Preliminary titration

A sample was added to 100 ml of water and mixed to dissolve the substance under determination. 1 ml of iodate(V), starch solution and 10 ml of iodide solution were added and determined with hydrochloric acid in drops approximately every 5 seconds until the first navy blue tint was obtained.

Final titration

A sample, 1 ml of iodate(V) and starch solution and 10 ml of iodide solution as well as the titrant in an established amount, reduced by about 2 ml, were added to 100 ml of water. The titration was carried out with hydrochloric acid as above. The amount of titrant, used in the final titration, was reduced by an amount used in blank test.

Table 1. The titration of active substances in selected pharmaceutical preparations (comparison method).

Preparation	$\bar{x}$		s		Confidence interval		Coefficient of variability %		Test F $\alpha = 0.05$	Test T $\alpha = 0.05$
	JJ	FPV	JJ	FPV	JJ	FPV	JJ	FPV		
Phenobarbitalum natrium	0.9865	0.9906	0.0063	0.0038	0.0045	0.0027	0.63	0.38	2.75	1.67
Cyclobarbitalum calcium	0.1970	0.2012	0.0023	0.0015	0.0016	0.0011	1.17	0.75	2.35	6.95
Sulfacetamidum natrium	50.4	48.7	0.3432	0.2625	0.25	0.19	0.68	0.54	1.71	11.07

JJ – the method for establishing the end-point based on the iodate(V)–iodide reaction.
FP V – according to the Polish Pharmacopoeia V.

Phenobarbitalum natrium – the ratio of active substance under examination to the weighed amount is presented. Cyclobarbitalum calcium – the content of active substance in grams in the mean tablet weight (0.3511 g) is shown. Sulfacetamid natrium – the amount of active substance recalculated for one ampoule is presented.

The active agent content as declared by the producer: Cyclobarbitalum calcium – 0.2 g per tablet, Sufacetamid natrium – 50 mg per ampoule, Phenobarbitalum natrium – 100%.

Each preparation was tested 10 times. The active substances were also determined by employing the methods recommended in the Polish Pharmacopoeia V (FP V). The results are presented in Table 1.

DISCUSSION AND CONCLUSIONS

The method presented above is much simpler than the bromatemetric one (Cyclobarbitalum Calcium) and requires no extraction and troublesome drying to constant mass (Phenobarbitalum Natrium). The sizes of samples taken for analysis are considerably smaller than those required for the pharmacopoeiah methods, while the differences in precision can be neglected (Test F). The T values indicate that the differences in average results in both methods are statistically significant. In case of Phenobarbitalum natrium and Sulfacetamidum natrium, the average values in the developed method are closer to the declared values. In case of Cyclobarbitalum calcium, the FP V method gives value closer to the declared average. Some previous tests have indicated that the method can be used for titration of salts of weak acids of $pK > 6$. In many cases the method is competitive for titration in anhydrous medium. The higher values of standard deviation (s) for JJ result from considerably smaller size of samples taken for analysis compared to those used in the methods recommended by FP V. The application of both methods is set up by the lower limit (FP V) and the upper limit (JJ) due to required titrant concentrations.

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Received: 18.09.2001