Asian Journal of Chemistry Vol. 18, No. 1 (2006), 497–502

Constant Current Coulometric Determination of Some Phenothiazine Drugs in Pharmaceutical Preparations

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A rapid amperostat-coulometric method has been described for the microgram level determination of some phenothiazine derivatives in pharmaceutical preparations. The method is based on estimation of these derivatives by determining the amount of electrolytically generated bromine required to react stoichiometrically with these drugs present in the solution. In case of each drug progressively smaller quantities are estimated and minimum quantity that can be estimated with reasonable accuracy is determined. Further, a systematic error analysis in the estimation of these derivatives by this method is also carried out.

Key Words: Coulometry determination, Phenothiazine drugs.

INTRODUCTION

Phenothiazine derivatives make valuable pharmacological preparations. Owing to their versatile pharmacological actions, they are widely used in therapeutics, particularly as psychotropic drugs[1-3]. In view of their importance, considerable work has been done on their estimation[4-7]. In literature, various analytical methods are available for determination of these drugs[8-14].

In the present paper, a rapid, accurate and sensitive constant current coulometric method for the determination of promethazine theoclate and prochlorperazine mesylate is described. The method is based on the electrochemical generation of bromine with 100% current efficiency and its rapid quantitative reaction with promethazine theoclate and prochlorperazine mesylate. This method has been applied to determine microgram level quantities of these drugs in tablets.

EXPERIMENTAL

Promethazine theoclate and prochlorperazine mesylate used were from May & Baker (India) Ltd., Mumbai. The drugs were used without any further purification for the determination. All other chemicals used were of analytical grade from S.D. Fine Chemicals.

Coulometric Cell: The cell[15] consists of platinum foil as working electrode. In a separate compartment a silver spiral was used as the auxiliary electrode. There was provision for indicator electrode system which indicated the generated

bromine concentration and consisted of platinum tip indicator electrode and saturated calomel electrode (SCE) as reference electrode. In the cell there was provision for nitrogen inlet and outlet to carry out estimation in inert atmosphere of nitrogen. The cell was mounted on magnetic stirrer to stir the solution under study.

Current measurements: The electrolytic current for bromine generation was noted by means of fine 100 μA.

Time measurements: Time measurements were carried out by using a stop watch by means of which the time could be measured accurate to a second.

Indicator electrode system: The platinum tip indicator electrode and the SCE were connected through a moving coil galvanometer. The sensitivity of the galvanometer was 7.15×10^{-9} amp/mm deflection.

Stock solutions: Potassium bromide (0.1 M) solution was prepared by dissolving the required amount of potassium bromide in 1 L of double distilled water. 0.5 M sulphuric acid solution was prepared by diluting 28.0 mL of concentrated sulphuric acid to 1000 mL by double distilled water. Promethazine theoclate (4.0×10^{-4} M) stock solution was prepared by dissolving an Avomine tablet containing 20 mg of promethazine theoclate in double distilled water and diluting to 100 cm^3. Prochlorperazine mesylate (2.2×10^{-3} M) stock solution was prepared by diluting 10 cm^3 Stemetil vial containing 125 mg prochlorperazine mesylate to 100 cm^3 by double distilled water.

Procedure

Bromine was generated at platinum foil working electrode by passing a current of 100 μA through the cell and the applied working electrode potential was 0.75 V *vs.* SCE. The concentration of the bromine generated was directly proportional to the deflection of the galvanometer. Since the drug reacted with the generated bromine, there would be decrease in the concentration of the bromine which reflected on the galvanometer deflection. Therefor,e it was necessary to note down galvanometer deflection before the addition of drug. After noting the deflection, the drug was added and bromine generation was continued until the deflection reached the initial value. The time required for this was noted. The number of millicoulombs passed was calculated from time and current passed through the cell.

The number of bromine atoms reacting with each molecule of promethazine theoclate and prochlorperazine mesylate was determined by taking known amount of drug. Then the unknown amount of drug samples were estimated by calculating the number of millicoulombs passed.

Each estimation was repeated five times. The repetitions were carried out by adding same amount of the sample to the generated bromine after noting down the initial galvanometer deflection each time.

RESULTS AND DISCUSSION

Bromine was electrogenerated at platinum working electrode by applying a potential of 0.75 V *vs.* SCE. Simultaneously hydrogen was evolved at the auxilliary electrode. The electrogenerated bromine reacted rapidly with promethazine theoclate and prochlorperazine mesylate even at very low concentrations.

It has been already emphasized in all the reports on coulometric estimations that the reagent should be electrogenerated with 100% efficiency and also that it should react stoichiometrically with the compound to be estimated. However, a less known fact in coulometric estimation is that the electrogenerated reagent also should react rapidly with the compound to be estimated. In absence of such rapid reactions, the electrogenerated reagent accumulates in the system reacting slowly with the compound. In the meanwhile, the indicator electrode senses the presence of free electrogenerated reagent and therefore gives a false estimation. There it is absolutely necessary that electrogenerated reagent besides fulfilling the commonly expected qualities should also react rapidly with the compounds to be estimated, so that there will be no false indications of the completion of the reaction.

It was quite essential to know the number of bromine atoms reacting with each molecule of promethazine theoclate and prochlorperazine mesylate. By knowing constant current passed and time, the number of millicoulombs passed was calculated. From number of millicoulombs, the number of electrons participating in the reaction was determined. This indirectly gives the number of bromine atoms participating in the reaction. It was observed that 6 bromine atoms were reacting with each molecule of the drug. After knowing the bromine atoms reacting with the drug molecule, the estimations of these drugs were carried out.

The lowest possible amount of promethazine theoclate that could be estimated was 7.5 μg. The estimations were carried over a range of 8–80 μg by repeating each estimation five times. The error analysis showed that the root mean square error (RMSE) was below one microgram and relative root mean square error (RRMSE) was below 0.6 (Table-1).

In case of prochlorperazine mesylate, the lowest amount that could be estimated was 5 μg. Repeated estimations were carried out over a range of 5–125 μg. In this range the RMSE worked out to be below 0.9 μg and RRMSE was below 0.15 (Table-2).

In order to ensure that this method was correctly estimating the amount of drug in sample, with no significant influence from the other constituents of the composition of the commercial preparation, estimations of these drugs were carried out in their pure form. The results were in satisfactory agreement with the expected values. Therefore, the other constituents of these commercial preparations were not seriously interfering with the estimations of these compounds by constant current coulometry.

TABLE-1
CONSTANT CURRENT COULOMETRIC ESTIMATION OF PROMETHAZINE THEOCLATE

Amount of Promethazine theoclate (μg)	No. of esti-mations	Duration of current passed (s)	No. of millicoulomb passed	Amount of promethazine theoclate estimated (μg)	RMSE* (μg)	RRMSE†
8	1	85	8.5	7.3	0.638	0.079
	2	85	8.5	7.3		
	3	90	9.0	7.8		
	4	88	8.8	7.4		
	5	87	8.7	7.5		
16	1	178	17.8	15.3	1.025	0.064
	2	186	18.6	16.0		
	3	171	17.1	14.7		
	4	176	17.6	15.1		
	5	173	17.3	14.9		
32	1	369	36.9	31.8	0.604	0.019
	2	373	37.3	32.1		
	3	383	38.3	33.0		
	4	365	36.5	31.5		
	5	380	38.0	32.4		
48	1	564	56.4	48.6	0.667	0.014
	2	569	56.9	49.0		
	3	559	55.9	48.2		
	4	554	55.4	47.7		
	5	549	54.9	47.3		
64	1	738	73.8	63.6	0.779	0.012
	2	748	74.8	64.4		
	3	740	74.0	63.7		
	4	753	75.3	64.9		
	5	730	73.0	62.9		
80	1	933	93.3	80.4	0.572	0.007
	2	923	92.3	79.5		
	3	939	93.9	80.9		
	4	928	92.8	80.0		
	5	926	92.6	79.7		

*Root mean square error
†Relative root mean square error

TABLE-2
CONSTANT CURRENT COULOMETRIC ESTIMATION OF PROCHLORPERAZINE MESYLATE

Amount of promethazine mesylate (μg)	No. of esti-mations	Duration of current passed (s)	No. of millicoulombs passed	Amount of Prochlorperazine mesylate estimated (μg)	RMSE* (μg)	RRMSE†
5	1	62	6.2	6.1	0.0751	0.150
	2	56	5.6	5.5		
	3	59	5.9	5.8		
	4	51	5.1	5.0		
	5	55	5.5	5.4		
15	1	160	16.0	15.7	0.620	0.041
	2	159	15.9	15.6		
	3	152	15.2	14.9		
	4	145	14.5	14.2		
	5	155	15.5	15.2		
25	1	244	24.4	23.9	0.871	0.035
	2	267	26.7	26.1		
	3	259	25.9	25.3		
	4	254	25.4	24.8		
	5	249	24.9	24.3		
50	1	526	52.6	51.4	0.904	0.018
	2	576	57.6	50.5		
	3	506	50.6	49.5		
	4	511	51.1	50.0		
	5	521	52.1	50.9		
75	1	768	76.8	75.1	0.712	0.010
	2	758	75.8	74.1		
	3	763	76.3	74.6		
	4	760	76.0	74.3		
	5	763	76.3	74.6		
100	1	1022	102.2	100.0	0.648	0.006
	2	1020	102.0	99.2		
	3	1025	102.5	100.2		
	4	1021	102.1	100.0		
	5	1026	102.6	99.6		
125	1	1275	127.5	124.7	0.545	0.004
	2	1280	128.0	125.1		
	3	1275	127.5	124.7		
	4	1285	128.5	125.6		
	5	1270	127.0	124.2		

*Root mean square error
†Relative root mean square error

Sources of Error

The main source of error in the estimations of promethazine theoclate and prochlorperazine mesylate by electrogenerated bromine is the voltage fluctuation in power supply which caused non-uniformity in the stirring. This changed the galvanometer deflection and caused error.

Conclusion

The estimation of these drugs by constant current coulometry with electrogenerated bromine is relatively simple and reasonably accurate. Further, the number of chemicals required is small in each case. The apparatus is also simple and inexpensive. The time required for each analysis is about 20 min. Therefore, it is a good method for routine pharmaceutical analysis of these compounds.

REFERENCES

1. P.G. Ramappa, H. Sanke Gowda and A.N. Nayak, *Analyst*, **105**, 663 (1980).
2. S.L. Bhongade and A.V. Kasture, *Talanta*, **40**, 1525 (1993).
3. P. Nagaraja and J. Seetharamappa, *Indian J. Pharm. Sci.*, **57**, 68 (1994).
4. K.C.S. Murthy and J. Seetharamappa, *Indian J. Pharm. Sci.*, **62**, 273 (2000).
5. A.G. Sajjan, J. Seetharamappa and M.B. Melwanki, *Indian J. Pharm. Sci.*, **63**, 61 (2001).
6. P. Nagaraja and J. Seetharamappa, *Indian J. Pharm. Sci.*, **57**, 68 (1995).
7. S.L. Bhongade and A.V. Kasture, *Indian J. Pharm. Sci.*, **55**, 151 (1993).
8. N.V. Pathak, I.C. Shukla and S.R. Shukla, *Talanta*, **29**, 58 (1982).
9. J.J. Mollinger and C.E. Keeler, *Anal. Chem.*, **36**, 1840 (1964).
10. F.H. Merkle and A.C. Discher, *Anal. Chem.*, **36**, 1639 (1964).
11. L. Laiten, I. Bello and P. Gaspar, *J. Chromatogr.*, **156**, 327 (1978).
12. F.W. Teare and R.N. Yadav, *Can J. Pharm. Sci.*, **13**, 69 (1978).
13. L.F.S. Chagonda and J.S. Millership, *Analyst*, **113**, 233 (1998).
14. A.C. Mehta, *Analyst*, **106**, 1119 (1981).
15. J. Bassette, R.C. Denney, G.H. Jeffery and J. Mendham, in: A.I. Vogel's Text Book of Quantitative Inorganic Analysis, 4th Edn., ELBS-Longman, London (1982).

(*Received*: 21 March 2005; *Accepted*: 3 October 2005) AJC-4430