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Determination of Paracetamol in pure form and in dosage forms using *N*,*N*-dibromo dimethylhydantoin

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Abstract

Paracetamol (Acetaminophen) is one of the most frequently used analgesic drugs. At therapeutic dosage levels the drug is relatively non-toxic. Because of its increasing therapeutic use, its assay and quality control are of vital importance. A number of methods, including instrumental [1–4] and titrimetric [5–7], are available for the quantitative determination of paracetamol in literature. A simple and accurate titrimetric method has been developed for the assay of paracetamol in pure form and in dosage forms, using *N*,*N*-dibromo dimethylhydantoin (DBH). Though a number of N-halo compounds are available for the determination of pharmaceuticals [8–10], DBH has greater advantages over such reagents [11]. © 1997 Elsevier Science B.V.

Keywords: Titrimetry; Paracetamol; *N*,*N*-dibromo dimethylhydantoin; Amaranth indicator

1. Experimental

1.1. Reagents

N,*N*-dibromo dimethylhydantoin (DBH) was prepared by brominating dimethylhydantoin. A standard solution (≈ 0.01 M) was prepared in water as reported previously [11].

Pure paracetamol obtained as a gift sample from Kerala State Drugs and Pharmaceuticals, Alleppey, Kerala, India, was further purified by recrystallization from ethanol and then used.

Paracetamol tablets such as Calpol (Burrough Wellcome India, Bombay), Crocin (Duphar Interfran, Bombay), Fepanil (Citadal Fine Pharma. Madras), Ifimol (J.B. Chemicals and Pharmaceuticals, Ankaleshwar), Maliden's (Nicholas Laboratories India, Bombay), Medomol (Medopharm, Madras), Metacin (Themis Pharmaceuticals, Gujarat), Metaplus (Surajman's Enterprices, Daman) and Pyrigesic (East India Pharmaceuticals, Calcutta) purchased from the local market were taken for analysis. Twenty tables were accurately weighed and finely powdered. A known mass (≈ 0.15 g) of the powder was dissolved in 50 ml of aqueous acetic acid (10% v/v). The solution was filtered through a Whatman 41 filter paper; the residue was washed five times with aqueous acetic acid solution (10% v/v) and the combined filtrate and washings were made up to 250 ml. Pure paracetamol sample (≈ 0.15 g) was also made into a solution in aqueous acetic acid (10%

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Table 1
Determination of Paracetamol (pure)

	Range (mg)	Equivalence No.[a]	Recovery[a] (%)	R.S.D.[a] (%)
DBH method	2.31–5.07	3.99	99.7	0.8
Pot. ferricyanide method	2.31–5.07	3.97	99.0	0.8
Spectrophotometric method	2.31–5.07	3.99	99.7	0.7

[a]Average of six replicate determinations.

v/v). Amaranth indicator solution (0.2% w/v) was prepared in ethanol.

2. Procedure

To a measured volume (5–15 ml) of the sample solution, two drops of amaranth indicator were added. This was titrated with standard DBH solution. The end point was the disappearance of the pink colour. From the titre value the amount of paracetamol was calculated from the equation

$$W = \frac{M \times V \times N}{n} \text{ mg}$$

where M is the relative molecular mass of paracetamol, V is the volume of DBH of normality N, consumed and n is the equivalence number (here it is 4).

3. Results and discussion

Typical results of the titrations of paracetamol (pure) are presented in Table 1. From an examination of Table 1, it is revealed that 1 M of paracetamol consumed 4 equivalents of DBH. Table 2 gives a detailed data on the analysis of paracetamol formulations with DBH. The presently developed method has been compared with the reported ferricyanide method [7] (titrimetric) and also the official method [4] (spectrophotometric) and the results are included in Table 2. To check the validity of the developed method, recovery studies have also been carried out on two typical tablets viz. Metaplus and Metacin and the findings are presented in Table 3.

In all these titrations, paracetamol is oxidised to p-quinone, consuming 4 equivalents of DBH M^{-1} of paracetamol (Fig. 1). The formation of this product is confirmed by product analysis. Solutions of paracetamol and DBH were mixed in bulk amounts in the stoichiometric ratio. The product formed was extracted in carbon tetrachloride. Excess solvent was evaporated and it was dried under vacuum. The purity of the product was checked by TLC. Melting point of the product was found to be 115°C which is more or less same as the melting point of p-quinone (116°C). With a nitrogen detection test, the purified compound showed a negative result. IR spectrum of the product showed a sharp band at 1650 cm^{-1} which can be assigned for a C=O bond. These observations support the fact that the titration product is p-quinone. The formation of this product is further confirmed by mixed melting point determination and by Co-IR.

The proposed method is superior to the existing titrimetric methods. The potassium ferricyanide method [7] is time consuming while the existing sodium methoxide [5] method requires strictly anhydrous condition. The reported bromine method [6] faces the difficulties due to the unstable nature of the reagent. A close examination of Table 1 and Table 2 reveals that the developed method is better in accuracy and precision. Table 2 explains that the presently developed titrimetric method is better in accuracy and precision than the reference titrimetric method and at the same time comparable with the official instrumental method. From the recovery data, it can be seen that the presently developed method is reliable and reproducable (Table 3). Common tablet excipients like starch, lactose, talc, etc will not interfere with the titrations. The use of DBH is advantageous because it

Table 2
Determination of Paracetamol in different tablets

S. No.	Tablet	Maker's specification (mg/tablet)	DBH method		Pot. ferricyanide method		Spectrophotometric method	
			Paracetamol found[a] (mg/tablet)	R.S.D.[a] (%)	Paracetamol found[a] (mg/tablet)	R.S.D.[a] (%)	Paracetamol[a] (mg/tablet)	R.S.D.[a] (%)
1	Calpol	500	497	0.9	498	0.8	497	0.7
2	Crocin	500	498	0.7	500	0.5	499	0.7
3	Fepanil	500	498	0.8	494	1.3	498	0.8
4	Ifimol	650	649	0.9	651	0.9	650	0.9
5	Maliden's	500	493	0.9	493	1.2	495	0.8
6	Medomol	500	500	0.4	500	0.5	499	0.5
7	Metacin	500	488	0.9	492	1.2	490	0.6
8	Metaplus	650	655	0.6	646	0.9	653	0.5
9	Pyrigesic	500	500	0.9	497	1.3	501	0.7

[a]Average of six replicate determinations.

Table 3
Recovery studies on two tablets

Tablet taken (amount taken)	Paracetamol added (mg)	Paracetamol found (mg)	Recovery (%)
Metaplus (5.95 mg)	0.48	0.47	98
	0.95	0.98	103
	1.43	1.45	101
	1.90	1.92	101
Metacin (6.03 mg)	0.48	0.47	98
	0.95	0.93	98
	1.43	1.40	98
	1.90	1.89	99

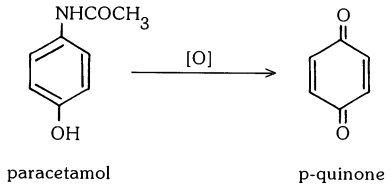

Fig. 1.

is cheap, readily available, easy to handle and is highly soluble in water.

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References

[1] S.F. Belal, M.A.H. Elsayed, A. Elwality and H. Abdine, Analyst, 104 (1979) 919–921.
[2] K.K. Verma and A. Jain, Talanta, 32 (1985) 238–240.
[3] J.L. Hamilton, J. Assoc. Off. Anal. Chem., 54 (1971) 895–897.
[4] British Pharmacopoeia H.M. Stationary Office, London, 341 (1973).
[5] H. Affalion, N. Keim and M. Streresscue, Rev. Chim., 11 (1982) 14–18.
[6] K. Satiadarma, S. Tino and T. Hermini, Acta. Pharm. Indones., 10 (1985) 37–38.
[7] M.K. Srivastava, D. Singh, S. Ahamed and I.S. Shukla, Zh. Prikl. Khim., 57 (1984) 901–904; Chem. Abstr., 101 (1984) 60205.
[8] K. Girish Kumar and P. Indrasenan, Analyst, 113 (1988) 1369–1372.
[9] K. Girish Kumar and P. Indrasenan, Talanta, 37 (1990) 269–272.
[10] K. Girish Kumar and R. Jayashree, J. Pharm. Biomed. Anal., 11 (1993) 165–168.
[11] K. Girish Kumar and L. Karpagaselvi, Analyst, 119 (1994) 1375–1377.