THE FLASK COMBUSTION TECHNIQUE IN PHARMACEUTICAL ANALYSIS: IODINE-CONTAINING SUBSTANCES

BY C. A. JOHNSON AND C. VICKERS

From the Analytical Development Group, Standards Department, Boots Pure Drug Co. Ltd.

Received May 27, 1959

The flask method for combustion of organic samples has been applied to a number of iodine-containing substances of pharmaceutical interest including the non-staining iodine ointments. The method is both rapid and simple and the accuracy and precision of the results obtained show that it is suitable for routine control purposes and possibly for consideration as an official assay procedure.

THE flask combustion technique has aroused considerable interest since the application of the principle was revived by Schöniger in 1955[1]. The method has been used for the determination of many types of substances[2] but to date there has been no attempt to apply it to materials of pharmaceutical interest. The iodine-containing substances of the British Pharmacopoeia and British Pharmaceutical Codex form a group of materials to which the method might be applied with advantage. The flask combustion method described below is simpler and more rapid than the present official methods and an assessment of its applicability, precision and accuracy therefore seemed desirable.

EXPERIMENTAL

The method recommended is applicable to all the substances examined and is based on that described by Schöniger[1,3].

Apparatus. The apparatus consists of a stout-walled 500-ml. iodine flask of resistant glass. Into the stopper is fused one end of a length of platinum wire about 13 cm. long and 1 mm. in diameter. To the free end is attached a piece of 36 mesh platinum gauze measuring $1\frac{1}{2} \times 2$ cm. (Fig. 1).

Reagents. These should be of analytical reagent grade wherever possible. *Bromine solution.* Dissolve 100 g. of potassium acetate in glacial acetic acid, add 4 ml. of bromine and dilute to 1 litre with glacial acetic acid. *Formic acid. Potassium iodide. Sodium hydroxide* N. *Sodium thiosulphate* 0·02 N and 0·01 N. Prepared when required from 0·1 N sodium thiosulphate which has been standardised against potassium iodate. *Starch mucilage* of the B.P. appendix II B.

Method. Accurately weigh a suitable quantity of the sample by difference and transfer to a strip of filter paper (Whatman No. 1 is suitable) which has been folded into three along its length. A convenient size has been found to be 3×5 cm. but this is not critical, provided that both sample and paper burn satisfactorily during the subsequent combustion stage. Enclose the sample in the filter paper by folding in the outer thirds and rolling up the strip. Grip the small packet so obtained in the platinum gauze and insert a narrow strip of filter paper into the roll to act as a fuse.

Moisten the ground glass joint of the flask with water and fill the flask with oxygen after adding 10 ml. of water and 2 ml. of N sodium hydroxide. Ignite the fuse and immediately insert the stopper into the flask. Since a small positive pressure is formed during combustion, hold the stopper firmly in place. Once the sample is burning vigorously turn the flask on its side so as to prevent incompletely burned material from falling out of the gauze into the liquid. As soon as the combustion is complete shake the flask vigorously for about 5 minutes; then place a few ml. of water in the collar of the flask and withdraw the stopper, when the slight negative pressure will suck the water in to wash down the neck. Rinse the stopper, platinum wire, gauze and walls of the flask with distilled water. Add an excess (5–10 ml.) of bromine solution and allow to stand for 2 minutes. Remove the excess bromine by addition of formic acid (about 0·5–1·0 ml.), wash down the sides of the flask with water and sweep out any bromine vapours above the liquid with a current of air. Add 1 g. of potassium iodide and titrate with 0·02 (or 0·01) N sodium thiosulphate, using starch mucilage as indicator.

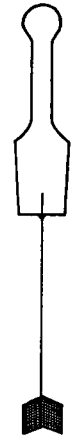

FIG. 1. Stopper with platinum wire and gauze attached as used in the flask combustion method.

With ointments, the sample is weighed on to a small square of greaseproof paper which is folded so as to completely enclose the material and is then itself folded in filter paper as usual. In some instances a small amount of carbon may deposit on the wall of the flask during combustion but this does not appear to affect the result.

Schöniger[1] suggested a technique whereby the method might be applied to the assay of liquid samples. A glass capillary was used to hold the sample and this was wrapped in paper and then broken immediately before ignition. Some workers[4,5] have made use of gelatin capsules to hold the liquid but in our experience methylcellulose capsules are preferable, since these burn without "spitting" and do not give rise to nitrogenous combustion products. The liquid sample is weighed into one end of the capsule, a piece of rolled filter paper is added to act as an absorbent, the capsule is closed, wrapped in filter paper and ignited as usual.

RESULTS AND DISCUSSION

The method was first tried on *o*-iodobenzoic acid of micro-analytical reagent grade (theoretical iodine content 51·17 per cent) and was shown to give satisfactory recoveries (Table I).

Table I also lists the results obtained on a number of iodine-containing substances used in pharmacy. It will be seen that the mean values obtained by the Flask method and results by the official method (which in each case is that described in the appropriate B.P. or B.P.C. monograph) are in good agreement. Results obtained by two operators showed that the range obtained using the flask method was in most assays

somewhat wider than that using the reference method. To make a more thorough assessment of the variation to be expected when using the flask method three official substances of different type were chosen for special study. The results obtained are listed in Table II. In our

TABLE I

RESULTS OBTAINED BY THE OFFICIAL METHOD AND THE FLASK METHOD ON VARIOUS IODINE-CONTAINING SAMPLES

Substance	Results by official method	Results by flask method			
		Analyst	No. of determinations	Mean	Range
Iodobenzoic Acid ..	51·17 per cent I (Theory)	1 2	9 5	51·1 51·1	50·9–51·2 50·9–51·3
Chiniofon Sodium B.P.	99·1 99·2	1 2	6 4	99·1 99·0	98·9–99·3 98·7–99·4
Di-iodohydroxyquinoline B.P.	98·1 98·3	1	3	98·3	98·1–98·5
Iodoform B.P.C. ..	99·9 100·3	1 2	3 3	99·9 99·8	99·8–100·2 99·7–100·0
Iodoxyl B.P. (I)* ..	85·8; 85·8 85·7; 85·8	1 2	4 3	85·7 85·6	85·2–85·9 85·5–85·7
Iodoxyl B.P. (II) ..	100·0	1	3	100·1	100·1–100·2
Iopanoic Acid B.P. ..	99·3 99·4	1 2	4 2	99·3 99·2	99·1–99·5 99·1–99·2
Pheniodol B.P. ..	99·1	1 2	4 4	98·9 99·0	98·7–100·1 98·7–100·2
Thyroxine Sodium B.P.†	90·2	1 2	5 3	90·2 90·3	90·1–90·5 90·2–90·4
Propyliodone B.P. ..	100·1 100·0	1 2	4 4	100·0 100·0	99·9–100·0 99·8–100·1
Ethyl Iodophenylundecanoate B.P.C.	100·0 100·0	1	3	100·2	100·1–100·3
Tablets of Diiodohydroxyquinoline B.P. ..	0·195 g./tab.	1 2	3 3	0·196 g./tab. 0·197 g./tab.	0·195–0·196 0·197–0·198
Tablets of Pheniodol B.P.C.	0·479 g./tab.	1	3	0·479 g./tab.	0·478–0·480
Iodised Oil Injection B.P.	39·9 per cent I. 40·2 (by fusion)	1	6	40·3	39·9–40·5
Chiniofon B.P. 1948 ..	29·6 per cent I	1	2	29·6	29·4–29·8

All the above determinations were made using 0·02 N sodium thiosulphate and sample weights varying between 10 and 25 mg. to give a titre of about 20 ml. according to iodine content. Results are expressed as per cent compound unless otherwise stated.

* Old and discoloured sample. † Calculated with reference to original material.

opinion these figures show that the method is suitable for routine control purposes, and might be acceptable as an official assay procedure subject to its satisfactory application in other laboratories.

The results obtained on various batches of non-staining iodine ointments are particularly interesting. Although reproducible results were obtained by the flask combustion method (except in Batch 3) it appeared that there was no relation with the B.P.C. method. In view of this the zinc reduction method (B.P.C. 1949, Supplement 1952) and a modified B.P.C. method were also applied. Results by the three comparison

methods showed considerable differences but results by the flask technique were in close agreement with those obtained by the modified B.P.C. method. The figures obtained by the flask method on Batch 3 showed a considerable spread and, in view of the agreement on other samples, it was concluded that the batch was not homogeneous. After the batch had been reworked good agreement was obtained. Duplicate determinations on non-staining iodine ointments can be made within 40 minutes.

TABLE II

A COMPARISON OF THE PRECISION OF THE FLASK AND OFFICIAL METHODS FOR THREE B.P. SUBSTANCES

Substance and method	No of results	Mean results	Range	Standard deviation
Thyroxine Sodium				
Flask	18	90·3	90·1–90·6	0·146
Official	6	90·2	90·1–90·3	0·077
Pheniodol				
Flask	24	99·0	98·7–99·2	0·161
Official	6	99·1	99·0–99·2	0·100
Propyliodone				
Flask	20	100·0	99·7–100·2	0·151
Official	6	100·1	100·0–100·2	0·089

TABLE III

RESULTS OBTAINED BY THE FLASK AND THREE OTHER METHODS ON NON-STAINING IODINE OINTMENTS

Batch No.	Analyst	Results (per cent Iodine)				
		By Flask combustion (50 mg. sample 0·01 N $Na_2S_2O_3$)		Zinc reduction (B.P.C. Supp. 1952)	B.P.C.	Modified B.P.C.*
			Mean			
1	1	5·10; 5·10; 5·09; 5·06;	5·09	4·90	4·98	5·07
	2	5·11; 5·09; 5·11; 5·10;	5·10	4·92	5·00	
2	1	5·25; 5·23; 5·24; 5·26;	5·25	5·04	5·15	5·24
				4·98	5·08	
3†	2	5·43; 5·80; 6·21; 5·39;		5·25		5·38; 5·52
3 (resample)		5·52; 5·38; 5·54; 5·36;				
3 (reworked)		5·47; 5·44; 5·49; 5·50;	5·48			5·46
4†	1	5·05; 5·03; 5·00; 5·03;	5·03	4·73	4·72	4·99
				4·75	4·74	4·99

* Sample and sodium carbonate packed in two crucibles as for Chiniofon Sodium B.P.
† Batches 3 and 4 contained methyl salicylate.

When the work was started it was considered possible that, because of the small weight of material used for a determination, slight variations in uniformity of samples might significantly affect the results; in practice this was not found out to be the case. All the assays listed above were carried out on routine control samples which had not been pre-treated in any way. The ability of the method to detect non-uniformity in samples so rapidly may be turned to advantage as was demonstrated with the Iodine Ointment.

REFERENCES

1. Schöniger, *Mikrochim. Acta*, 1955, 122.
2. Macdonald, *Industr. Chem. Mfr.*, 1959, **35** (1), 33.
3. Schöniger, *Mikrochim. Acta*, 1956, 869.
4 Lysyj and Zarembo, *Analyt. Chem.*, 1958, **30**, 428.
5 Corner, *Analyst*, 1959, **84**, 41.

After Mr. Vickers presented the paper there was a DISCUSSION.