THE ASSAY OF MERCURIC SALICYLATE

By M. DOMBROW

From the Chelsea School of Pharmacy

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THE iodometric method of assaying mercuric salicylate of the British Pharmaceutical Codex, 1934, was replaced in the Fourth Supplement by a thiocyanate titration of the mercury. The organic matter is destroyed by oxidation with potassium permanganate, first in alkaline then in acid solution and excess of oxidising agent is removed by adding ferrous sulphate solution.

Several other standard procedures for the determination of mercury in organic compounds or in the presence of organic matter follow the same principle, but oxidation is usually effected by heating with a mixture of nitric and sulphuric acids.[1, 2, 3] While it is accepted that salicylates and other phenols can be oxidised by permanganate, there is no specific information in the literature on the oxidation of mercuric salicylate. The composition of this salt has not yet been established and though it is described as a salt of salicylic acid in which the mercury replaces both the phenolic and carboxylic hydrogen atoms[4], the composition varies with the method of preparation and the B.P.C. allows material containing between 54 and 59·6 per cent. of mercury.

It was found in a preliminary experiment that a carefully homogenised sample assayed differently by the B.P.C. and United States Pharmacopœia XI methods. The latter employs a nitric-sulphuric acid oxidation followed by a thiocyanate titration of the mercury. The results differed by 1·27, representing a divergence of over 2 per cent. of the mercury. The mercury content of the sample was established gravimetrically by decomposing the sample with boiling hydrochloric acid and precipitating as sulphide. The precipitate was filtered, washed and dried to constant weight. A carbon disulphide extraction showed that no sulphur had been precipitated. The results were in close agreement with the U.S.P. figures: B.P.C. method, 56·30 per cent.; U.S.P. XI method 57·57 per cent.; sulphide method 57·55 per cent. (mean of 3 determinations).

BRITISH PHARMACEUTICAL CODEX METHOD

Dissolve 0·3 g. of sample in 10 ml. of 0·1N sodium carbonate. Add 1·5 g. of finely powdered potassium permanganate in small portions and mix well. After 5 minutes add carefully 5 ml. of sulphuric acid and after a further 5 minutes, 40 ml. of water and then acid solution of ferrous sulphate in small quantities, shaking after each addition until the precipitate is dissolved. Add 5 ml. of nitric acid and titrate with 0·1N ammonium thiocyanate, using ferric ammonium sulphate as indicator.

Acid Solution of Ferrous Sulphate. Freshly prepared by dissolving 7 g. of ferrous sulphate in 90 ml. of water, freshly boiled and cooled, and adding sulphuric acid to 100 ml.

Thiocyanate Titration Conditions

The acidity and amount of indicator added in the titration conform to established usage[5,6,7,8], but about 70 ml. of ferrous sulphate solution is required to dissolve the manganese dioxide precipitate, introducing ferric ion equivalent to 8·5 g. of ferric ammonium sulphate or 85 ml. of indicator solution. Variation of the indicator concentration has been found of little significance over a small range[8], but the total ferric concentration here is far above any hitherto tested. Furthermore, the sensitivity of the end-point is reduced in the strongly-coloured solution.

The quantitative effect was determined by titrating a standard solution of mercuric nitrate with thiocyanate at the same final mercury concentration and acidity as in the B.P.C. method using (a) 90 ml. of indicator, (b) 5 ml. of indicator and 85 ml. of water; results: (a) 17·50 ml.; (b) 17·65 ml.

The end-point, taken as the first definite brownish colour, was premature and represented a loss of 1 per cent. on the low burette reading. This accounts for part, at least, of the deficiency shown.

In all subsequent work, the ferrous sulphate solution was replaced by 3 per cent. hydrogen peroxide, added in small portions until the solution was clear; excess of peroxide was removed with 10 per cent. permanganate solution, added to the first permanent pink and decolorised with a small crystal of ferrous sulphate. The suitability of this modification was verified by titrating standard mercuric nitrate with thiocyanate (a) alone (b) in the presence of a solution prepared by carrying out a blank determination on salicylic acid, using the modified method. Identical results were obtained.

Quantity of Permanganate

The bulk of the oxidation occurs in alkaline solution, a heavy brown precipitate of manganese dioxide being thrown down immediately on adding permanganate. The solution becomes purple when all the permanganate has been introduced and the colour and precipitate remain until the reducing agent is added. The excess of permanganate is small since the purple colour fails to develop on increasing the weight of sample by less than 10 per cent.

The relation between sample weight/permanganate ratio and completeness of oxidation was studied in a series of determinations in which the weight of permanganate was fixed at 1·5 g. and the weight of sample varied from 0·2 to 0·45 g. The results were calculated in terms of burette reading per g. of sample.

Reduction of the sample weight below 0·3 g. had no effect on the recovery, whereas from 0·32 g. upwards, low and erratic results were obtained. An adequate safety margin was established by using 2 g. of permanganate, with which recoveries were fully maintained up to 0·4 g. of sample.

Time and Temperature of Oxidation

Increasing the alkaline oxidation time to 25 minutes had no significant effect (Table I). The importance of the acid oxidation stage is shown by the added recovery on increasing the severity of the conditions. Whilst a longer period than the 5 minutes oxidation of the B.P.C. method gave by itself no advantage, due probably to the rapid fall of temperature in the initial few minutes, a higher recovery was obtained on heating the solution for 10 minutes (Table I).

TABLE I

Conditions of oxidation			Mercury per cent.
Alkaline soln.	Acid soln.	Temp. effect	
25 minutes	5 minutes	Not heated	57·32
5 „	1 „	„	56·94
5 „	5 „	„	57·44
5 „	10 „	„	57·43
5 „	5 „	Heated	57·45
5 „	10 „	„	57·59
5 „	20 „	„	57·59

Losses During Acidification

Acidification with sulphuric acid produces violent effervescence; the liquid boils and purple fumes are given off. Cooling is rapid in 5 minutes, owing to the relatively large surface area of the small volume of liquid. It was found that 10 ml. of 50 per cent. sulphuric acid gave a strong and more prolonged heat effect and enabled the reaction to be easily controlled, with little spray and no fuming. Recoveries were comparative both with the unheated solutions and on heating for 10 minutes, as suggested in the previous section. Results: sulphuric acid B.P. unheated 57·44 per cent., heated 10 minutes 57·59 per cent.; sulphuric acid (50 per cent.) unheated, 57·43 per cent., heated 10 minutes, 57·57 per cent.

Modified Method

Dissolve 0·3 g. of sample, accurately weighed, in 10 ml. of N (approx.) sodium carbonate. Add in small portions 2 g. of finely powdered potassium permanganate and mix well. After 5 minutes, add carefully 10 ml. of sulphuric acid (50 per cent.) and boil the solution gently for 10 minutes. Cool, add 40 ml. of water and then hydrogen peroxide solution (3 per cent.) in small portions until the precipitate is dissolved. Add potassium permanganate solution (10 per cent.) until the solution becomes a faint permanent pink, decolorise with a small crystal of ferrous sulphate, add 5 ml. of nitric acid and titrate with 0·1N ammonium thiocyanate solution using ferric ammonium sulphate solution as indicator.

The modified method was examined on a range of samples of varying mercury content (Table II), and found to agree closely with the U.S.P. XI and sulphide methods.

Table II also shows that the precision of the modified method is higher than that of the U.S.P. XI and B.P.C. methods.

TABLE II

Sample	Mercury per cent.			
	B.P.C. method	Modified method	U.S.P. XI method	Sulphide method
1	54·53 54·62	55·65 55·67	55·72 55·65	55·55
2	55·29 55·19	56·49 56·44	56·49 56·43	56·45
3	55·98 55·93	57·08 57·11	57·15 57·08	56·99
4	56·29 56·25 56·36	57·57 57·59 57·56	57·68 57·59 57·44	57·57 57·49 57·59
5	57·08 57·04	58·38 58·41	58·44 58·34	58·32
6	58·18 58·29	59·48 59·53	59·51 59·51	59·48

SUMMARY

1. The B.P.C. assay of mercuric salicylate has been shown to give low results, compared with the U.S.P. XI method and a gravimetric sulphide method.

2. A study of the conditions of the B.P.C. method has been made and sources of error revealed.

3. A modification of the B.P.C. method has been proposed which gives results in agreement with the sulphide and U.S.P. XI methods.

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REFERENCES

1. Rupp and Nöll, *Arch. Pharm.*, 1905, **243,** 1.
2. Schulek and Floderer, *Z. anal. Chem.*, 1934, **96,** 388.
3. *United States Pharmacopœia* XI.
4. Remington, *Practice of Pharmacy, 9th Ed.*, 1948, 550.
5. Rupp and Krauss, *Ber. dtsch chem. Ges.*, 1902, **35,** 2015.
6. Low, *Chemist-Analyst,* 1919, **29,** 13.
7. Kolthoff and Stenger, *Volumetric Analysis,* 1942, Interscience, New York, Vol 2.
8. Karaoglanov, *Z. anal Chem.*, 1943, **125,** 406.