

# A NEW COMPLEXOMETRIC METHOD FOR THE DETERMINATION OF SOME SULPHONAMIDES

BY H. ABDINE AND W. S. ABDEL SAYED

*From Pharmaceutical Chemistry Department, Faculty of Pharmacy,  
University of Alexandria*

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A complexometric method for the determination of some sulphonamides has been evaluated. The sulphonamides are precipitated as cupric salt, filtered and the excess copper is titrated with EDTA using PAN as indicator.

THE different methods for the determination of some sulphonamides were reviewed by Abdine and Abdel Sayed (1962). They include diazotisation, electrometric, bromometric, neutralisation and non-aqueous titration methods. Sulphonamides can also be determined by precipitating with metallic ions, example silver, mercuric or copper ions and completing the determination gravimetrically or volumetrically in aqueous or non-aqueous media, see, for example, Lapiere (1946, 1947, 1948).

The application of a complexometric method seemed to hold possibilities, the sulphonamides being quantitatively precipitated by a measured excess of metallic ions and the excess (in the filtrate) titrated complexometrically. Copper was chosen, because silver ions cannot be directly titrated complexometrically (Flaschka, 1953) and mercury ions necessitate special precautions lest basic salts of variable composition precipitate (Partington, 1950).

## EXPERIMENTAL

The sulpha drugs are practically insoluble in water. Sulphadiazine was chosen initially and was dissolved in dilute sodium hydroxide solution,\* and treated with a known excess of standard copper solution. The excess copper in the filtrate was determined complexometrically. The results obtained were high compared with the official (B.P. 1958) electrometric method.

The effect of changing the time of standing of the precipitate before filtration and of changing the pH of the precipitation was investigated.

### *Effect of Time of Standing*

Sulphadiazine (0.4 g.), accurately weighed, was dissolved in the minimum amount of 0.1N sodium hydroxide (pH 9) then 0.1M copper sulphate solution (30 ml.) was added slowly with constant stirring. The solution was filtered immediately or after standing for 15 to 30 min. The precipitate was washed with distilled water and the filtrate and washings completed to 250 ml. An aliquot of 50 ml. was taken, 60 ml. ethanol (to improve the end-point) (Cheng and Bray, 1955), 10 ml. buffer solution

\* Dissolving the sulphadiazine in dilute acids or dilute ammonia prevented its precipitation with copper.

pH 6, drops of PAN indicator were added and the solution was titrated with 0.02M EDTA.

The results obtained were calculated on the basis of a 2:1 ratio of sulphonamide to copper according to Lott and Bergeim (1939), Lapiere (1948) and Billman, Jonetos and Cheinin (1960).

In the determination, filtering immediately gave a per cent recovery (mean of three determinations) of 104.03 (+1.83 - 1.91), after standing 15 min. this was 107.43 (+1.35 - 1.04), and after standing 30 min. this was 116.04 (+1.09 - 0.92). The B.P. 1958 per cent recovery was (average of three determinations) 99.71 (+0.32 - 0.34).

#### *Effect of pH*

The high results, even when filtration was immediate, may be due to co-precipitation of copper ions at the relatively high pH of the precipitation (pH 9). Trials were therefore made to adjust the solution to lower pH values with buffer solutions at pH 8, 7, 6.5, 6, 5.5 (borax buffers) and 4 (acetate buffer) respectively, added before the solution was filtered.

In the determination at pH 8 the per cent recovery (mean of three determinations) was 102.62 (+0.75 - 0.5), at pH 7 this was 102.28 (+1.69 - 1.52), at pH 6.5, 101.02 (+0.33 - 0.42), at pH 6, 99.18 (+0.14 - 0.07), at pH 5.5, 97.62 (+0.5 - 0.54), and at pH 4 this was 86.89 (+1.31 - 1.02). The B.P. 1958 mean result = 99.71 per cent. The above results show that pH 6 is the most suitable for the precipitate. The solution is stable at pH 6 for about 15 min.

#### *The Recommended Procedure*

Weigh accurately 0.4 g. of sulphadiazine and dissolve in the minimum amount of NaOH (0.1N), (faint blue to thymol blue). Add 0.1M copper sulphate (30 ml.) and borax buffer solution pH 6 (20 ml.). After filtration wash the precipitate with distilled water to a total volume of filtrate and washings of 250 ml. Take an aliquot (50 ml.) add absolute ethanol (60 ml.) and 3 to 4 drops of PAN indicator and titrate the solution with 0.02M EDTA until green.

Some comparative results are given in Table I.

Sulphaguanidine and sulphanilamide do not give a precipitate with a silver or copper ions.

#### *Reagents*

*Copper sulphate:* 0.1M; 24.971 g. of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ , per litre, was standardised with 0.1M EDTA by the method of Flaschka and Abdine (1956) using PAN.

*Edta disodium salt* (of the B.P. 1958): 0.1M, standardised with 0.1M zinc solution using Eriochrome black T.

*Zinc solution:* 0.1M, 6.538 g. AR metallic zinc dissolved in the minimum amount of hydrochloric acid AR and diluted to 1 litre.

*Pan:* 1-(2-pyridyl azo-2-naphthol) 0.1 per cent in methanol.

Acetate buffer solution pH 4: 27.22 g. sodium acetate + 40 ml. N HCl per litre.

DETERMINATION OF SOME SULPHONAMIDES

TABLE I

RESULTS OF ASSAY OF SOME SULPHA DRUGS BY DIFFERENT METHODS

Sulpha drug	B.P. 1958 method	Argentimetric titration*	Complexometric method
	per cent found	per cent found	per cent found
Sulphadiazine .. .. .	99.71 (+0.32 - 0.34)	98.19 (+0.38 - 0.22)	99.65 (+0.36 - 0.33)
Sulphathiazole (Non-official) ..	99.35 (+0.27 - 0.29)	98.85 (+0.23 - 0.27)	98.36 (+0.19 - 0.34)
Sulphadimidine .. .. .	99.26 (+0.38 - 0.36)	98.87 (+0.25 - 0.30)	99.11 (+0.46 - 0.43)
Sulphamerazine .. .. .	99.66 (+0.27 - 0.30)	99.56 (+0.25 - 0.43)	99.81 (+0.56 - 0.49)
Sulphapyridine (Non-official) ..	99.65 (+0.36 - 0.22)	99.30 (+0.42 - 0.37)	99.56 (+0.25 - 0.34)
Sulphacetamide sodium .. .. .	99.45 (+0.32 - 0.36)	Soluble silver salt	77.82 (+3.22 - 3.34)

\* Lee Kum-Tatt, 1957.

*Borax buffers*: solution A: 31 g. boric acid + 8.75 g. sodium chloride per litre. Solution B: 2.86 g. sodium carbonate per litre.

Buffer solution pH 5.5: 300 ml. solution A + 6 ml. solution B.

Buffer solution pH 6: 300 ml. solution A + 12.5 ml. solution B.

Buffer solution pH 6.5: 300 ml. solution A + 50 ml. solution B.

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