

## SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; Glenn L. Jenkins, John C. Krantz, Jr., Heber W. Youngken, L. W. Rowe, L. W. Rising, C. O. Lee, E. V. Lynn, W. G. Crockett.

### THE SULPHUR OINTMENTS AND THEIR ASSAY.\*<sup>1</sup>

BY CHARLES E. BRADY AND HENRY M. BURLAGE.<sup>2</sup>

#### INTRODUCTION.

The United States Pharmacopœia and the National Formulary recognize three ointments containing elemental sulphur in the sublimed form: (a) Sulphur Ointment, U. S. P., which is a simple mixture of sublimed sulphur (15% by weight) and benzoinated lard; (b) Alkaline Sulphur Ointment, N. F., a more complex mixture of sublimed sulphur (20% by weight),  $K_2CO_3$ , water and benzoinated lard and (c) Compound Sulphur Ointment, N. F., a still more complex ointment containing sublimed sulphur (15% by weight), precipitated  $CaCO_3$ , cade oil, soft soap and lard.

Since the U. S. P. and the N. F. serve as legal standards for maintaining the strength and purity of official medicaments it seems desirable to have a satisfactory assay for these three ointments.

#### PROPOSED METHODS.

Methods which oxidize the S to  $H_2SO_4$  and subsequent precipitation with  $BaCl_2$  test solution are tedious and difficult to apply to pharmaceutical preparations containing sulphur, especially the ointments. Of the oxidation methods that have been especially applied to these ointments are those of Evers and Elsdon (1). The ointment is heated with a mixture of concentrated  $HNO_3$  and  $Br_2$  and the excess of the latter removed, diluted with water and the aqueous solution extracted with ether to remove the fat; or a mixture of  $Br_2$  and  $NaOH$  may be used to bring about the oxidation. Both procedures are tedious and in general give low results.

Simple methods employing organic solvents to separate the fatty material and other ingredients from the sulphur cannot be applied as sulphur is appreciably soluble in most organic solvents. This has been proved by Henville (2) and substantiated by work done in our laboratories.

Attention was, therefore, turned from the usual long oxidation-gravimetric methods to those involving volumetric procedure. In 1932 Castiglioni (3) proposed the conversion of the sulphur contained in acetone extracts of rubber into thiocyanate by boiling with KCN solution under a reflux and evaporating to dryness and the thiocyanate determined by Shulek's method (4) in which the excess of cyanide is converted to glycol nitrile by formaldehyde and then determined by titrating with standard  $AgNO_3$  solution in a solution acidified with  $HNO_3$ . Allport (5) investigated this method and found that it gave low results for ointments and modified the procedure by treating the sample with a reagent consisting of KCN (4)

\* Scientific Section, A. PH. A., Portland meeting, 1935.

<sup>1</sup> Pharmaceutical Laboratories, School of Pharmacy, University of North Carolina, Chapel Hill, N. C.

<sup>2</sup> Professor of Pharmacy, School of Pharmacy, University of North Carolina.

Gm.), and triethanolamine (90 cc.) dissolved in H<sub>2</sub>O (*q. s.* to 1000 cc.) and refluxing in the presence of soft paraffin and pumice to convert the S to KCNS, adding 0.1*N* AgNO<sub>3</sub> and titrating the excess with 0.1*N* ammonium thiocyanate using ferric alum as an indicator.

In 1934 Fleck and Ward (6) proposed the following method which they claim to be shorter than that of Allport's and is not affected by sulphates. The material is refluxed with a solution of Na<sub>2</sub>SO<sub>3</sub> to convert the S quantitatively to Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and the excess sulphite removed by the addition of HCHO and acetic acid and the thio-sulphate titrated by 0.1*N* iodine solution using starch as an indicator. Soft paraffin is added as in the previous method to accelerate the reaction. Work in our laboratories did not substantiate the claims of Allport and of Fleck and Ward with regard to the accuracies and brevities of time claimed for their methods.

In 1933 Shulek (7) proposed a method for the determination of sulphur in sulphur-bearing drugs whereby the sample is treated with KCN in the presence of a small amount of H<sub>2</sub>O and acetone converting the S into KCNS and after boiling with boric acid, the thiocyanate is determined volumetrically by the method of the same author (8). This investigator found that in slightly acid solutions alkali cyanides and thiocyanates with bromine water forms cyanbromide quantitatively according to the reaction:  $\text{HCNS} + 4 \text{Br}_2 + 4 \text{H}_2\text{O} = \text{H}_2\text{SO}_4 + 7 \text{HBr} + \text{CNBr}$ , the latter compound being stable in acid solution. The excess of bromine is removed by the addition of phenol which does not react with CNBr in the course of 3-4 hours. Potassium iodide is then added which reacts with CNBr in acid solution to liberate iodine as follows:  $\text{CNBr} + 2 \text{HI} = \text{HCN} + \text{HBr} + \text{I}_2$ . The latter substance may be determined by titration with 0.01-0.1*N* sodium thiosulphate using starch as an indicator. Our investigations show that this method could be used for the determination of elemental sulphur in ointments when modified as follows:

"Weigh accurately into a small beaker (50 cc. capacity) a sample of ointment equivalent to 0.02-0.04 Gm. of S. Distribute on the sample about 0.2 Gm. KCN, add 8-10 drops of water and 15 cc. acetone and evaporate to dryness at a temperature sufficiently high to melt the ointment. Repeat the process of warming with acetone and follow by subsequent evaporation twice, using each time 5 cc. of acetone (or until all of the sulphur has been converted). Dissolve the residue in water and filter through a small filter. Heat the fatty material remaining in the beaker with 5 cc. of water almost to boiling, cool somewhat and pass the aqueous liquid through the same filter. Repeat this procedure 3-4 times. The combined filtrates are received in a 125 cc. glass-stoppered Erlenmeyer flask, add 1 Gm. of boric acid and boil gently for 10 minutes. (If a clear filtrate is not obtained, add the boric acid first and in some cases 0.5 Gm. coarse pumice may be necessary to accomplish this, boiling 10 minutes, filtering and washing the filter as described above.) Acidify the cooled solution (amounting to 50-60 cc.) with 5 cc. phosphoric acid (20%), add bromine water dropwise until the solution is distinctly yellow; add phenol (5%) until the solution is decolorized. Shake well and set aside for 1/4 hour; add 0.5 Gm. KI and allow to stand in the dark for 1/2 hour, keeping the flask securely stoppered, and then titrate in the usual manner with 0.1*N* Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> using *fresh* starch solution as an indicator. (1 cc. 0.1*N* Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> = 0.01603 Gm. S.)

#### EXPERIMENTAL.

Samples used in the investigation consisted of Sublimed Sulphur, U. S. P., of a commercial sample of Sulphur Ointment, U. S. P. (No. 1); a sample of sulphur ointment prepared in the laboratory according to the official directions (9)

(No. 1-A); alkaline sulphur ointment prepared according to the N. F. (10) (No. 2); Compound Sulphur Ointment prepared according to the N. F. (10) (No. 3) and a commercial sample stated to be twice the official strength for sulphur ointment (No. 3-A).

TABLE I.

Sublimed Sulphur, U. S. P.	Wt. of Sample.	Wt. Found.	% Purity.
	0.0203 Gm.	0.0201 Gm.	99.01
	0.0205	0.0205	100.00
	0.0217	0.0216	<u>99.54</u>
			Av. 99.52

TABLE II.

Preparation.	Sample No.	Series No.	Wt. of S Found.			
			Observer I.	Observer II.		
Sulphur Ointment (0.2 Gm. = 0.03 Gm. S.)	1	1	0.0300 Gm.	0.0303 Gm.		
			0.0304	0.0322		
			0.0291	0.0284		
				Av. 0.0298	0.0303	
		2	0.0303			
			0.0299			
			0.0296			
				Av. 0.0299		
		3	0.0293	Grand Average of All Detns. = 0.0299		
	0.0301					
	Av. 0.0297					
	1-A	1	0.0304	0.0318		
			0.0284	0.0282		
			Av. 0.0294	0.0300		
				0.0288	0.0311	
			0.0296	0.0307		
			0.0293			
			Av. 0.0292	0.0309		
			Grand Average of Series = 0.0298.			
Alkaline Sulphur Ointment (0.2 Gm. = 0.04 Gm. S)	2	1	0.0387	0.0390		
			0.0398	0.0388		
			0.0394			
			Av. 0.0393	0.0389		
					0.0399	Grand Average of the Series = 0.0392 Gm.
					0.0398	
					0.0388	
		Av. 0.0395				

## Compound Sulphur Ointment

(0.2 Gm. = 0.03 Gm. S)

3	1	0.0293	0.0295
		0.0292	0.0302
		0.0289	0.0295
		<hr/>	
		Av. 0.0291	0.0297
		Grand Average of Series = 0.0294 Gm.	
3-A	1		0.0655
			0.0663
			<hr/>
			Av. 0.0659

## SUMMARY.

1. A modification of Shulek's volumetric method for the determination of Sulphur in drugs is proposed for the assay of the official sulphur ointments.

2. The proposed method has been found to be applicable to the official ointments and is applied with promising results to samples of the three official ointments carefully prepared in the laboratory and to two commercial samples of which one was stated to be twice the official strength.

## BIBLIOGRAPHY.

- (1) Evers, N., and Elsdon, G. D., *Analyst*, 47, 199 (1922).
- (2) Henville, *Ibid.*, 55, 385 (1930).
- (3) Castiglioni, *Zeit. analyt. Chem.*, 91, 32 (1932).
- (4) Shulek, E., *Ibid.*, 65, 433 (1925).
- (5) Allport, N. L., *Quart. J. Pharm. Pharmacol.*, 6, 431-435 (1933).
- (6) Fleck, H. R., and Ward, A. M., *Ibid.*, 7, 178-181 (1934).
- (7) Shulek, E., *Pharm. Monatsh.*, 14, 228-229 (1933).
- (8) Shulek, E., *Z. analyt. Chem.*, 62, 337 (1923).
- (9) United States Pharmacopœia X, page 416.
- (10) National Formulary V, pages 269-270.

## A NOTE ON THE ASSAY OF MASS OF FERROUS CARBONATE.\*

BY JOHN C. KRANTZ, JR., AND C. JELLEFF CARR.<sup>1</sup>

## INTRODUCTION.

Based upon the work of Scott (1) and Knop (2), Krantz and Vidal (3) suggested the use of diphenylamine as an indicator in the titration of Mass of Ferrous Carbonate with tenth-normal potassium dichromate. This suggestion was adopted by the Revision Committee of the U. S. P. XI owing to the advantages offered by diphenylamine as an inside indicator, over potassium ferricyanide as an outside indicator.

The formation of the green chromic ion makes it somewhat difficult for the inexperienced worker to determine sharply the end-point of the titration. To obviate this difficulty, the present investigation was begun, with the aim to introduce the volumetric reagent, tenth-normal ceric sulphate solution, in place of the

\* Scientific Section, A. Ph. A., Portland meeting, 1935.

<sup>1</sup> Department of Pharmacology, School of Medicine, University of Maryland.