VOLUMETRIC ESTIMATION OF ATABRINE DIHYDROCHLORIDE AND RIVANOL LACTATE.

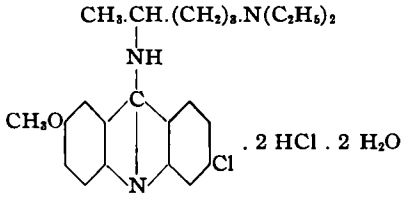
BY M. E. AUERBACH.*

The increasing application of acridine compounds in chemotherapy seems to make it advisable to acquaint investigators with a convenient method for the quantitative determination of two members of this class, namely: atabrine, which is of clinical interest in the therapy and prophylaxis of malaria; and rivanol, an internal antiseptic.

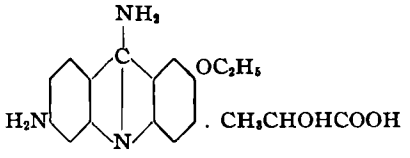
Atabrine and rivanol form difficultly soluble salts with a number of acids, *e. g.*, phosphotungstic, silicotungstic, hydriodic, salicylic, thiocyanic, ferricyanic, dichromic. Powell and Hall (1) have described a method for the determination of acriflavine which is based on the insolubility of the ferricyanic derivative. Of the atabrine and rivanol salts mentioned, however, the dichromic salt is the least soluble. Its formation has been made the basis of the method to be described, both for that reason and because it readily lends itself to a simple volumetric procedure.

FORMULAS.

Atabrine dihydrochloride is 2-chloro, 7-methoxy, 5-diethylaminopentyl amino acridine dihydrochloride. It normally occurs as the dihydrate:



Rivanol lactate is 3-ethoxy 5, 8-diamino acridine lactate:



MATERIALS USED.

The materials used were specially purified by recrystallization. The purity of the atabrine was checked by estimation of the bound HCl and water of crystallization, yielding the following figures:

Atabrine dihydrochloride (calc. from HCl)	93.20 per cent
Volatile at 100° C. (water of crystallization)	6.72 per cent

The purity of the rivanol was checked by a nitrogen determination (semi-micro Dumas):

Required for $(C_{15}H_{15}N_3O).CH_3CHOHCOOH$	12.24 per cent N
Found	12.36 per cent N

* Research Laboratories of the Winthrop Chemical Company, Inc., Rensselaer, New York.

METHOD.

0.10–0.30 Gm. are carefully weighed and introduced into a 100-cc. volumetric flask. Dissolve in 10–15 cc. water, add 10 cc. of a solution consisting of 260 Gm. sodium acetate and 280 cc. 30% acetic acid made to 1000 cc. Add 50 cc. 0.1N $K_2Cr_2O_7$, make up to the mark with water, mix well by transferring to a dry beaker and stirring, and filter through a dry Whatman No. 1 paper. Reject the first 15 cc. of filtrate. To 50 cc. of the subsequent filtrate in a glass-stoppered Erlenmeyer flask, add 13 cc. HCl (Sp. Gr. 1.10) and then 20 cc. 10% KI. Stopper quickly, mix by gentle swirling and let stand in the dark for two minutes. Back titrate with 0.1N $Na_2S_2O_3$.

$$50 - (\text{cc. } 0.1N\ Na_2S_2O_3 \times 2) = \text{cc. } 0.1N\ K_2Cr_2O_7 \text{ consumed}$$
$$1 \text{ cc. } 0.1N\ K_2Cr_2O_7 = 0.00787 \text{ Gm. Atabrine dihydrochloride}$$
$$= 0.01143 \text{ Gm. Rivanol lactate.}$$

A correction must be made to allow for the slight solubility of the precipitates, which are decomposed in acid solution, the dichromic acid portion then being back-titrated along with excess $K_2Cr_2O_7$. The following examples will make this clear:

I. *For Atabrine.*

	Weight Taken. (Reduced to Anhydrous.)	Cc. 0.1N $K_2Cr_2O_7$ Consumed.	Found (in Gm.).	Error (in Gm.).
A.	0.28212 Gm.	35.09	0.27616	−0.00595
B.	0.18667 Gm.	22.95	0.18061	−0.00606
C.	0.28183 Gm.	35.09	0.27616	−0.00567

The error is practically constant, allowing the final formula for percentage calculation to be written

$$\frac{(\text{Cc. } 0.1N\ K_2Cr_2O_7 \text{ consumed} \times 0.00787) + 0.006}{\text{Weight taken}} \times 100 = \text{per cent atabrine.2 HCl.}$$

II. *For Rivanol.*

	Weight Taken.	Cc. 0.1N $K_2Cr_2O_7$ Consumed.	Found (in Gm.).	Error (in Gm.).
A.	0.13621 Gm.	11.73	0.13407	−0.00214
B.	0.11380 Gm.	9.80	0.11201	−0.00179
C.	0.13661 Gm.	11.78	0.13464	−0.00197

Again, the error is practically constant, and the formula for calculation may be written

$$\frac{(\text{Cc. } 0.1N\ K_2Cr_2O_7 \text{ consumed} \times 0.01143) + 0.002}{\text{Weight taken}} \times 100 = \text{per cent rivanol lactic acid}$$

COMPOSITION OF ATABRINE AND RIVANOL DICHROMIC ACID SALTS.

The insoluble precipitates were washed well with water and alcohol, dried at 80° C. and then to constant weight at 100° C. Portions were then ignited to Cr_2O_3.

I.	Found, in the atabrine salt	16.86 per cent Cr
	Required for $C_{23}H_{30}N_3OCl.H_2Cr_2O_7$	16.84 per cent Cr.
II.	Found, in the rivanol salt	14.44 per cent Cr
	Required for $(C_{15}H_{15}N_3O)_2.H_2Cr_2O_7$	14.36 per cent Cr.

CONCLUSION.

A volumetric precipitation method has been described for the estimation of the acridine derivatives, atabrine dihydrochloride and rivanol lactate.

REFERENCE.

(1) Powell, A. D., and Hall, G. F., *Quart. J. Pharm. Pharmacol.*, 6, 389 (1933).