The Determination of Cyclamates in Sweetening Tablets

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The sulphate formed by the action of nitrous acid on cyclamates is determined by titration with standard alcoholic barium perchlorate solution after purification by ion exchange. The method has been applied successfully to determining cyclamate in mixed sweetening tablets, and saccharin does not interfere.

Cyclamate has been determined by direct titration with sodium nitrite solution using starch—iodide as external indicator[1]. This technique was improved by Richardson and Luton who detected the end point electrometrically[2]. Most of the methods, however, are based on the determination of one of the products of the nitrous acid—cyclamate reaction. Rees[3], and Richardson and Luton[4], measure by gas chromatography the cyclohexene produced in this reaction whilst the official method of the Association of Agricultural Chemists[5], and that of Davies[6], measure the sulphate produced, the former by the usual gravimetric procedure and the latter by titration of excess barium with E.D.T.A.

The semi-micro method of Fritz and Yamamura[7] is a very useful one for the direct volumetric determination of sulphate and it was thought that this might form the basis of a suitable method for cyclamates as an alternative to those already mentioned. In this method, interfering cations are removed from solution by passage through an ion-exchange column and a portion of the eluate is titrated with barium perchlorate solution using thorin as indicator. The sodium derived from the sodium nitrite was found to be satisfactorily removed by ion exchange but the nitrite seriously interfered with the titration. However, by boiling the eluate, the nitrite was readily destroyed and satisfactory titrations resulted.

Because of the importance of the ion exchange procedure and the relatively high concentration of cations in solution, it was necessary to ensure that the column was always sufficiently activated before use.

The method is equally applicable to calcium cyclamate, sodium cyclamate and cyclamic acid and, using the procedure described, it is possible to determine small quantities of these compounds conveniently and accurately. Satisfactory results were obtained when the method was applied to sweetening tablets containing both cyclamate and saccharin. Preliminary trials have shown that the method promises to be satisfactory also for determining cyclamates in soft drinks, and results of application of the method to this field are being collated.

Apparatus

1. Ion exchange column: Approximately 1·5 cm internal diameter, 20 cm long, with a tap, and containing Amberlite resin 1R—120(H) to a depth of 5 cm. The column is regenerated by treatment with 100 ml of 3 N HCl and washing with water, after each experiment.
2. Burette: 10 ml capacity with subdivisions of 0·02 ml.

Reagents

1. *Alcoholic barium perchlorate Soln.:* A 0·005 M solution. Dissolve 1·7 g of barium perchlorate in 200 ml of distilled water and dilute to 1 litre with Industrial Methylated Spirits (99 per cent.)
2. *Thorin Indicator:* Dissolve 0·2 g of 1-(*o*-arsonophenylazo)-2-naphthol-3:6-disulphonic acid, sodium salt (thorin) in water, and dilute to 100 ml.
3. *Sodium nitrite Soln.:* 10 per cent. in water.
4. *Sulphuric acid:* 0·01 N H_2SO_4 solution.

Method

STANDARDISATION OF THE BARIUM PERCHLORATE SOLUTION

Pipette 5·0 ml of 0·01 N sulphuric acid solution into a 100-ml conical flask. Add 20 ml of industrial methylated spirits (99 per cent.) and two drops of indicator. Titrate with the barium perchlorate solution, swirling the flask and contents vigorously throughout the titration. The end point is a delicate, but quite definite, change from yellow to pink and is seen best in good natural light; bright light and artificial light should be avoided.

From the titration result, calculate the factor F (mg per ml) for the perchlorate solution as follows:—

$$F = \frac{5{\cdot}0}{\text{titre}} \times 0{\cdot}896 \text{ for cyclamic acid}$$

$$\text{or} \begin{cases} \times\ 1{\cdot}006 \text{ for sodium cyclamate} \\ \times\ 1{\cdot}0815 \text{ for calcium cyclamate} \end{cases}$$

PROCEDURE FOR SWEETENING TABLETS

Dissolve an accurately-weighed quantity of the powdered tablets, equivalent to about 0·15 g of cyclamate, in distilled water. Add a small piece of litmus paper, and if necessary, dilute hydrochloric acid dropwise until the solution is just acid, and make up to 100 ml. Pipette 5 ml of this solution into a 100-ml, narrow-necked, conical flask, dilute with water to about 30 ml, and add 1 ml of sodium nitrite solution. Cover the neck of the flask with a watch glass, and boil the mixture gently for $1\frac{1}{2}$ minutes. Cool the solution, transfer it quantitatively to a 50-ml calibrated flask and dilute to the mark with water. Pass this solution through the ion exchange column, discarding the first 2×10-ml of eluate. Transfer 10 ml of the remaining eluate by pipette into a 100-ml, conical flask, and boil gently for $1\frac{1}{2}$ minutes taking care to avoid loss of contents by bumping. Cool the solution, add 40 ml of industrial methylated spirits (99 per cent.), two drops of indicator and titrate with the barium perchlorate solution as described under 'standardisation'. Record the titration (A ml).

Carry out a blank determination by repeating the above procedure using 5 ml of water in place of the 5 ml of prepared cyclamate solution. (B ml).

Using the factor found in the standardisation procedure, calculate the amount of cyclamate per tablet from the formula:—

$$\text{Cyclamate per tablet (mg)} = \frac{100\ F\ (A-B) \times W}{w}$$

where w = weight of sample taken,
and W = average weight of a tablet.

Control experiments

Solutions containing varying amounts of sodium cyclamate, saccharin sodium and sodium bicarbonate were prepared as follows:

Solution A: 0·2 g of sodium cyclamate in 100 ml of solution.

Solution B: 0·24 g of sodium cyclamate, 0·024 g of saccharin sodium, and 0·096 g of sodium bicarbonate in 100 ml of solution.

Solution C: 0·144 g of sodium cyclamate, 0·120 g of saccharin sodium and 0·096 g of sodium bicarbonate in 100 ml of solution.

Aliquots, each of 5 ml of these solutions, were taken for assay as above, and the results are shown in Table 1 on the basis of the equivalent amount of cyclamate present in the final solution which was titrated. The mean percentage recovery of these 12 results is 99·88 and the standard deviation 0·79. The results for solution B and C show that saccharin does not interfere with the determination.

TABLE I
RECOVERY OF CYCLAMATE FROM MIXED SWEETENERS

Solution	Quantity of Cyclamate present *milligrammes*	Quantity of Cyclamate found *milligrammes*	Recovery *per cent.*
A	2·0	1·97	98·7
	2·0	1·99	99·5
	2·0	1·99	99·5
	2·0	2·01	100·5
B	2·4	2·42	101·1
	2·4	2·34	97·5
	2·4	2·40	100·0
	2·4	2·41	100·5
C	1·44	1·45	100·8
	1·44	1·44	100·2
	1·44	1·43	99·5
	1·44	1·45	100·8

Blank values were determined, and in all cases were within the range 0·07 to 0·10 ml. For routine purposes, therefore, it should not be necessary to carry out a blank determination for each assay but an average value of 0·08 ml can be used, periodically checking that this is satisfactory.

Table II shows the results obtained on typical mixed sweetening tablets:

TABLE II
DETERMINATION OF CYCLAMATE IN SWEETENING TABLETS

Quantity stated *mg per tablet*		Quantity of Cyclamate found
Sodium cyclamate	Saccharin	*mg per tablet*
40	4	38·3
		38·7
50	5	48·9
		49·6
		48·3

References

1. "Sucaryl Sweetener in Soft Drinks: Technical Information". Abbott Laboratories Ltd.
2. Richardson, M. L., and Luton, P. E., *Analyst*, 1966, **91**, 522.
3. Rees, D. I., *Analyst*, 1965, **90**, 568.
4. Richardson, M. L., and Luton, P. E., *Analyst*, 1966, **91**, 520.
5. "Official Methods of Analysis of the Association of Agricultural Chemists" 10th Edition. Washington, D.C., 1965. p. 452.
6. Davies, A. M. C., *J. Assoc. Publ. Analysts*, 1966, **4**, 11.
7. Fritz, J. S., and Yamamura, S. S., *Anal. Chem.*, 1955, **27**, 1461.

Book Review

GAS CHROMATOGRAPHIC ANALYSIS OF DRUGS AND PESTICIDES. By BENJAMIN J. GUDZINOWICZ. Pp. 616 + ix. London. Edward Arnold Ltd., 1968. Price £13.

This book, first published in America in 1967, is Volume 2 in a series of monographs on Chromatographic Science. It is divided into two parts (1) the theoretical approach to Gas-Liquid Chromatography and (2) the analytical methods and technique as applied to drugs and pesticides.

The three chapters in Part 1 deal with *a.* the fundamentals of gas-liquid chromatography, general theory and principles, column efficiency, separating power and resolution, *b.* detectors—operating principles and theory, hydrogen flame ionization, argon ionisation, electron affinity and coulometric detectors, and *c.* qualitative and quantitative methods of analysis.

Part 2 concerns the application of gas-liquid chromatography to the analysis of drugs and pesticides. Eight chapters are devoted to drugs and pharmaceuticals. The subtitles of each chapter indicate the range of drugs examined:—phenothiazines and barbiturates, phenylethylamine-type and tryptamine-indole base alkaloids, morphine, nicotine, and pyrrolizidine-related alkaloids and marihuana cannabinols, antihistamines, high boiling amine anaesthetics and vitamins and a chapter on miscellaneous drugs and pharmaceuticals.

The final chapter in Part 2, comprising approximately one third of the volume, presents a wide coverage of the examination and analysis of pesticides, herbicides and related compounds including carbamates and triazines.

In the Analytical Section the Author has presented the results of numerous investigations carried out by many researchers in the fields of drugs and pesticides, from a non-theoretical approach and has included throughout the section a very comprehensive collection of data tables, and numerous illustrations of actual chromatograms.

Whilst the price of the book is rather high by average standards, the reviewer considers it to be an invaluable basic reference work with the added advantage that it is backed by a wealth of practical information. As far as Public Analysts are concerned, whether they are already involved in the application of gas-liquid chromatography to drugs and pesticides or are contemplating the purchase of this very versatile instrument, this book can be recommended as the analysts' Book of the Month.

(MISS) A. COOK.

THE LAW OF WEIGHTS AND MEASURES (SUPPLEMENT) By JOHN A. O'KEEFE. Pp. 80 + x. London; Butterworth and Co., 1967. Price 25s.

An extract from the Preface suitably describes the purpose of this volume, and reads—

"Since the *Law of Weights and Measures* was published in June 1966, there have been some new statutory provisions, interpretations by the High Court which affect the law in various ways and administrative directives from the Board of Trade which have added new procedures and clarified the actions to be taken in various contingencies.

"None of these particular matters is in itself of major importance, yet taken together the changes that they make in the law as stated in the main volume are of sufficient importance to make it necessary that it should be brought up-to-date. This the present supplement seeks to do and its aim is to correct and add to the principal volume so that together they present the position as at the 1st September 1967.

"The subject is one of constant concern to traders, administrators and the public and is particularly subject, in its flexibility, to changes in content and the elucidation of judicial decisions".

J. H. E. MARSHALL.