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Differential Electrolytic Potentiometric Titration of Vitamin C in Pharmaceutical Preparations

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ABSTRACT

The application of direct current differential electrolytic potentiometry for the aqueous titration of vitamin C has been investigated. The reaction of vitamin C with Ce (IV) is fast enough to permit its direct titration in 0.09 M sulfuric acid media. Cerium ammonium sulfate was used as a titrant and a couple of platinum electrodes as an indicating system. Titration curve shapes obtained are almost symmetrical with sharp peaks. The optimum current density was found to be 0.65 μA cm^{-2}. The procedure was applied successfully to the determination of vitamin C in commercial tablets, capsules as well as in juice in the concentrations of 0.02~10 ppm. The results of this study were favorably compared statistically with those obtained with official methods.

Key words: differential electrolytic potentiometry, oxidation titrimetry, vitamin C, cerium (IV), pharmaceutical preparations

INTRODUCTION

Vitamin C, better known as l-ascorbic acid, is classified as a carbohydrate and has the chemical structure of 1-keto-1-threo-hexono-γ-lactone-2,3-enediol. It is the enediol-group [-C(OH)=C(OH)-] which is responsible for the molecule's acidic and reducing properties[1]. Ascorbinometric titrations are a term earlier introduced in the literature by Erdey[1] in 1950 using vitamin C as a reductimetric titrant. Since then quite a number of titration procedures were adopted and classified into direct and indirect methods; the details of which were reviewed by Erdey and Svehla[1]. A titrimetric method, currently being used by the British Pharmacopoeia[2] for the assay of vitamin C in tablets using cerium (IV) as a titrant and ferroin sulfate indicator in sulfuric acid media, was described. In the same monograph, another titrimetric method for the assay of vitamin C generic form using iodine as a titrant and starch indicator in sulfuric acid media was offered[3]. Since then, numerous methods have been described for its determination involving the use of permanganate[1], gold (III) chloride[4], ferricyanide[5], *O*-iodosobenzoate(6), phenyl iodosoacetate[7], hexa-ammminecobalt (III) tricarbonatocobaltate[8], *N*-bromoimides[9], potassium bromate[10], and 2,6-dichloroindophenol[11]. The main sources of errors and limitations of the conventional titration procedures were found mainly in the use of indicators, location of the end point and complexity of reaction, thus encouraging the search for better alternative methods for the assay of this important drug.

The technique of direct current differential electrolytic potentiometry (d.c.DEP) consists of polarizing two identical electrodes with a stabilized small current and measuring the potential differences between them. The d.c.DEP technique has been applied to various types of titrimetric reactions in both aqueous[12-15] and non-aqueous media[16-20] using different types of electrodes.

Using this technique the polarized electrodes respond faster, the apparatus is simple and the salt bridge problems of the reference cell are eliminated. This paper describes oxidation reaction where vitamin C is being oxidized with Ce (IV). The applicability of d.c.DEP technique to the behavior of the polarized platinum electrodes is also reported.

MATERIALS AND METHODS

I. *Apparatus*

The constant current source which provides a stable current in the range 100 nA~100 μA was constructed. This source consists of a d.c. power supply, a rectifying unit, a filtering unit, and four integrated circuits. Platinum electrodes were checked according to a procedure described elsewhere[12,16]. The area of each electrode was measured and was found to be 1.53476 cm^2. The titration was undertaken by charging the cell with the electrolyte and connecting the electrodes to the constant current source.

II. *Materials and Reagents*

All solutions were prepared with double distilled water from reagent-grade materials. Ascorbic Acid Analar (BDH, Poole, Dorset, UK) stock solution was prepared daily by dissolving an accurately weighed quantity about 20 mg of ascorbic acid in water and diluted to 100 mL. Working solutions were prepared from the stock solution by dilutions.

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Standard cerium (IV) ammonium sulfate (0.096M; BDH, Poole, Dorset, UK) was prepared from Analar cerium ammonium sulfate which was dissolved in water containing 0.5516 M sulfuric acid. The solution was stirred, filtered then diluted to 1 L. This solution was standardized by titration with a standard solution of 0.1051 M di-ammonium iron (II) sulfate 6-hydrate, which was standardized by 0.05004 M potassium dichromate. The solution was diluted appropriately before use.

Sulfuric acid (GCC, UK) of 0.018387 M, 0.0919 M, and 0.1839 M were prepared by diluting Aristar grade sulfuric acid (98.0%) with water.

Tablets of Redoxon Orange 1000 (Roche, Basel, Switzerland) and Sedergine UPSA 200 (Rueil-Malmaison, France) were used. Capsules of Dentake (Eisai Co. Ltd., Japan) and Orange juice Zain (S.A.O.G., Oman) were used.

III. *Procedures*

(I) *Recommended Analytical Procedure*

An accurately measured volume of standard ascorbic acid solution containing 0.02~10 mg was transferred to the titration cell. Then, it was diluted to about 40 mL with 0.09193 M sulfuric acid solution. The platinum electrodes were immersed into the sample solution. The typical current density used was 0.65 μA cm^{-2}. The titration was done by running cerium ammonium sulfate solution from 10.0-mL micro burette, graduated at 0.02-mL slow intervals and constant stirring of the reactants was continued with an electromagnetic stirrer throughout the course of titration. The potential measurements were recorded at a stable reading after each addition. The exact volume of the titrant was read from graph, plotted between the values of ΔE (mV) and volume of the titrant.

(II) *Procedure for the Determination of Vitamin C in Dosage Forms*

Ten tablets containing ascorbic acid or the contents of 10 capsules were weighted and pulverized. An appropriate amount of the powder equivalent to 20 mg of ascorbic acid was dissolved in about 50 mL of water. It was left for 10 min in the dark to let the gases evaporated and the residue was filtered and washed 3~4 times with water, then was added about 5 mmol sulfuric acid. The mixture was made up to the mark with water in a 100-mL volumetric flask. An accurately measured volume of the solution was transferred and continued using the previously stated recommended analytical procedure.

(III) *Procedure for Determination of Vitamin C in Juice*

The appropriate volumes of the juice, which has a required amount of ascorbic acid, were taken directly and diluted with 20 mL of sulfuric acid solution (1 M) and 30 mL of water and diluted to 100 mL then continued using the previously stated recommended analytical procedure.

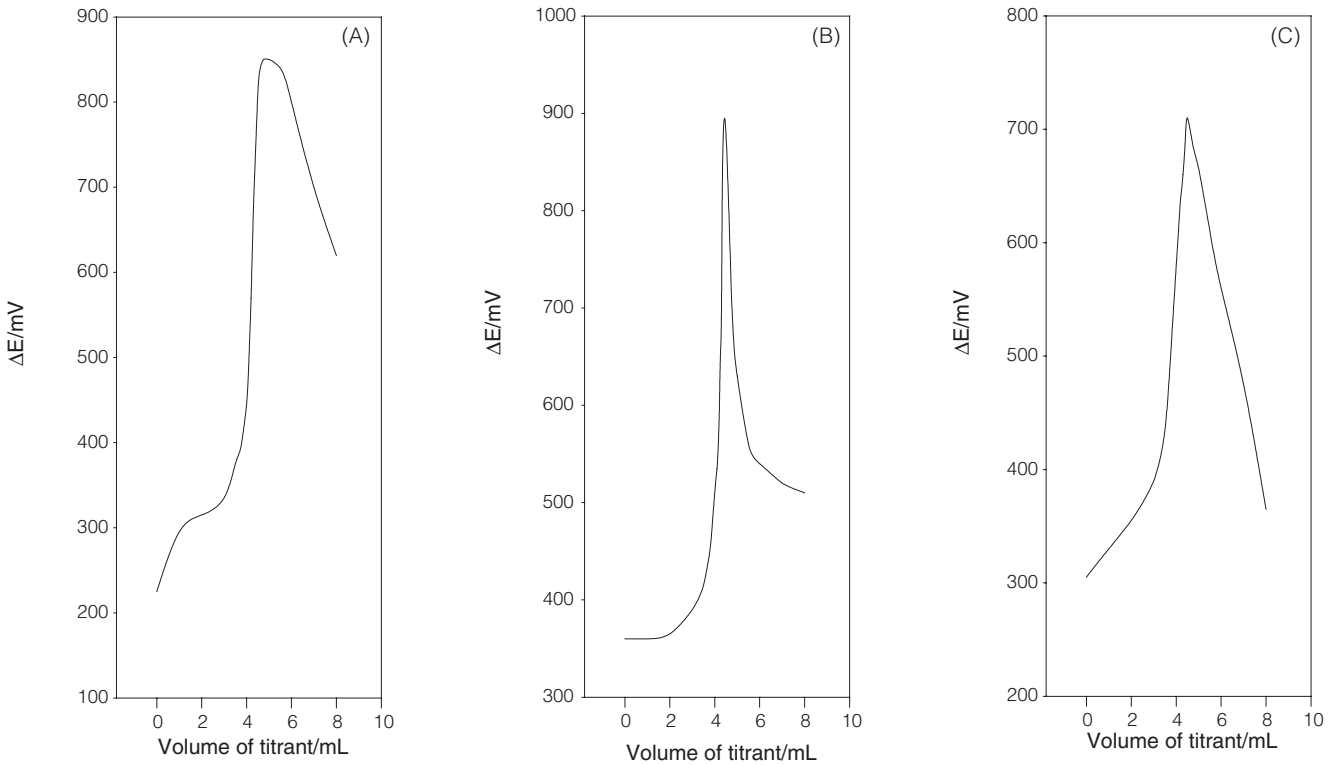

Figure 1. Titration of 2 mL of 1761.4 ppm vitamin C with 0.0096 M ammonium cerium (IV) sulfate using platinume electrode. Current density: 0.65 μA cm^{-2} in different concentrations of sulfuric acid. (A) 0.018 M, (B) 0.09 M and (C) 0.18 M sulfuric acid solutions.

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RESULTS AND DISCUSSION

I. *Chemical System and Optimization*

The method is based on the oxidation of vitamin C to the dehydroascorbic acid with cerium (IV) in sulfuric acid media through the following reaction:

$$2Ce^{4+} + C_6H_8O_6 \rightarrow C_6H_6O_6 + 2Ce^{3+} + 2H^+$$

The reaction kinetics has earlier been investigated[1] indicating that it is acid dependent. The reaction was found to be fast in low and slow in high acidic media[21].

If d.c.DEP is applied to follow the titration of ascorbic acid with cerium (IV) in sulfuric acid solution, a differential curve will be obtained and used to locate the end-point. The smoothness, the sharpness and the symmetry of the differential curve depend on the applying conditions, like the type of electrodes, the current density employed to polarize these electrodes, and the concentration of sulfuric acid solution. To investigate the conditions, several titrations were performed using platinum electrodes as an indicating system for this type of titrations. It was found that the differential curves are sharp, smooth and symmetric indicating the normal behavior of platinum electrodes. These electrodes were found to be suitable for this type of oxidation-reduction titration and they were employed in this work.

Other parameters that affect the shape of the DEP curve, like the current density, the concentration of sulfuric acid solution, and the concentration of the analyte, were also investigated. Six titrations were repeated by applying the current densities of 0.33, 0.65, 1.30, 1.95, 2.60 and 3.25 μA cm^{-2}. It was noted that an increase in the current density will result in an increase of the height of the resulting differential curve; however, the broadness of the peak will also increase. A current density of 0.65 μA cm^{-2}, which gives the best DEP curve, is considered an optimum one and was used during this study. Changing the concentration of sulfuric acid solution from 0.018 M to 0.18 M was found to have a significant effect on the shape of the DEP curve as shown in Figure 1. However, a smooth titration curve similar to the one shown in Figure 1B was obtained in a solution of 0.09 M sulfuric acid solution and was applied in all of the titrations. The sulfuric acid solution is used as a supporting electrolyte and it also enhances the response of the platinum electrodes by keeping them clean during the course of the titration.

Titrations were performed using different concentrations of vitamin C to examine the response of the applied electrodes and also to detect the lowest concentration that can be determined. The results of those titrations are shown in Figure 2 and the d.c.DEP curves can be easily used to locate the end-points. Concentrations of 0.02~10 ppm of vitamin C can be titrated by the d.c.DEP with good results in the pure vitamin C and its pharmaceutical preparations. Table 1 indicates the successful applicability of this technique.

A set of the normal titration curves obtained was shown in Figure 3. It is evident that comparable titration curves have resulted from the titration of vitamin C either in pure

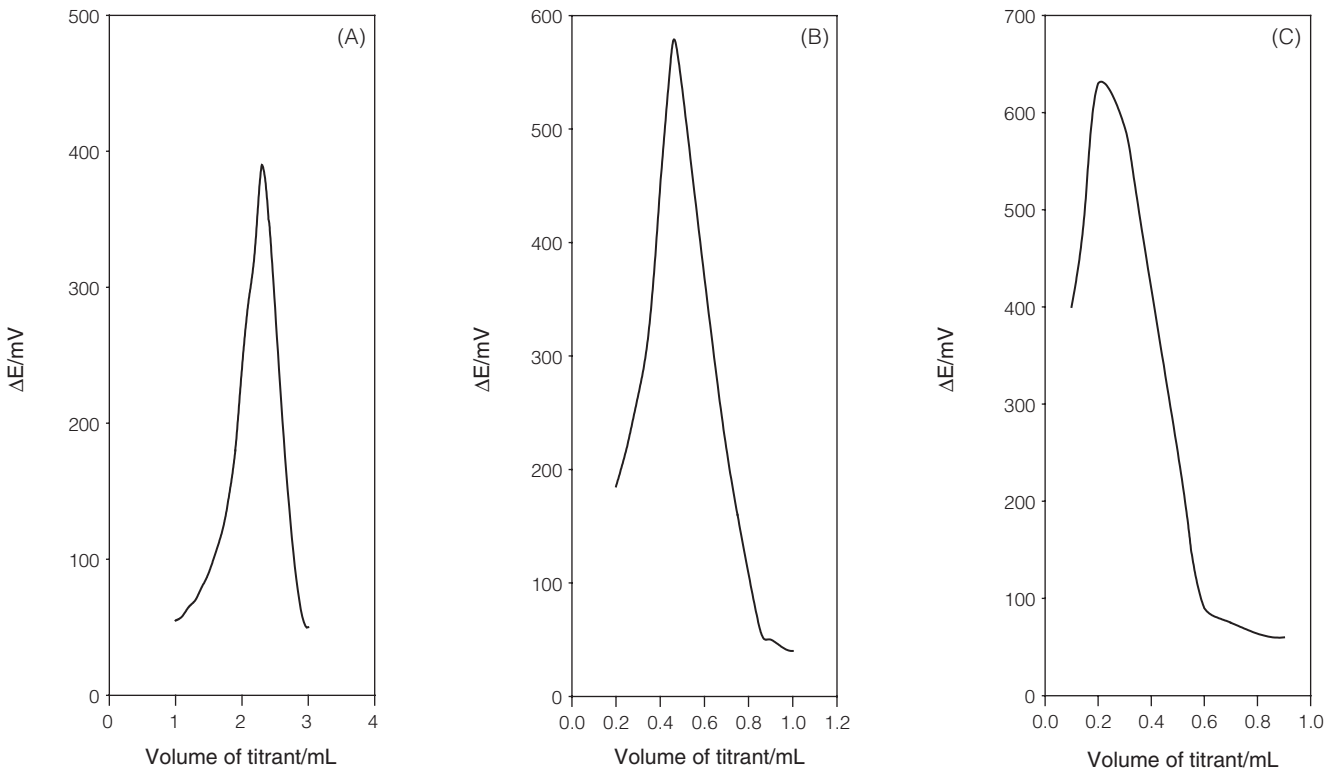

Figure 2. Effect of changing the concentration of vitamin C on the d.c.DEP differential curve at a current density of 0.65 μA cm^{-1} and sulfuric acid concentration of 0.09 M. Titration curves of 2.0 mL of (A) 880.70 ppm, (B) 176.14 ppm and (C) 88.07 ppm vitamin C with cerium (IV).

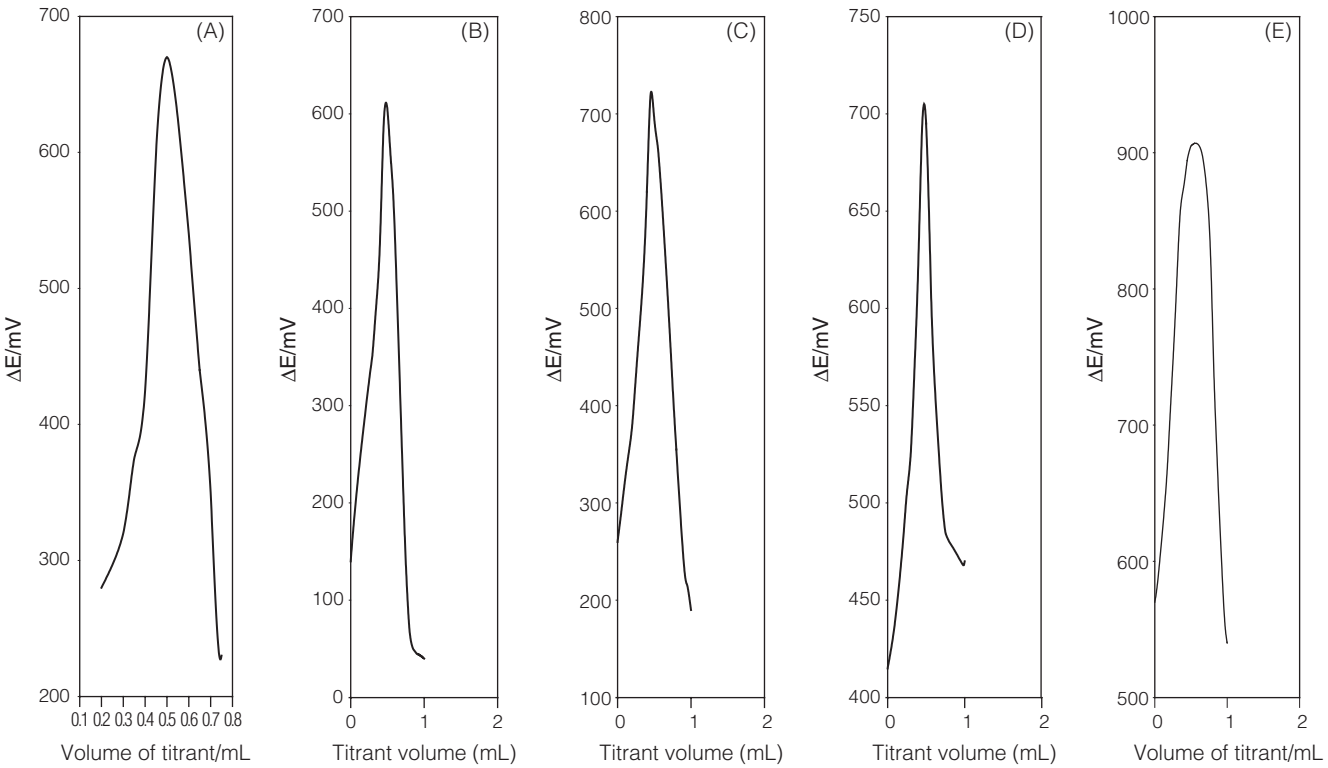

Figure 3. Titration of 2.0 mL of 200 ppm of each of (A) vitamine C, (B) Redoxon, (C) Dentake, (D) Sedergine and (E) orange juices with 0.0096 M cerium (IV) ammonium sulfate at a current density of 0.65 μA cm^{-2} and 0.09 M sulfuric acid concentration.

form or in the drug formulations. Similar solutions of pure vitamin C, Redoxon, Sedergine, Dentake and orange juice were found to require almost the same volumes of cerium (IV) to reach the corresponding end-points. This indicates that no interferences from the excipients of the drug formulations, such as calcium, citric acid, sugar, carbohydrates, vitamins B, ferrous fumerate, pantothenic acid, folic acid, acetylsalicylic, paracetamol, zinc and copper

Results for the determination of vitamin C in pure form and in its pharmaceutical preparations are compared with the results obtained by the official method[3] in Table 1. Statistical analysis between the two methods was performed and the Student's *t* value and variance ratio (F value) were calculated[22]. The results indicate no significant differences between the two methods with respect to accuracy and precision.

Compared with the official method, the proposed method is simple and requires small amounts of drug.

CONCLUSIONS

A simple and fast d.c.DEP method is proposed to the analysis of vitamin C in pure form, in its dosage forms, and in juices. The technique of d.c.DEP has the advantage over the previously reported methods with respect to specificity and sensitivity. It requires cheaper instrumentation and a simple electric circuit with only two platinum wire electrodes. The concentration range for its determination is lower than the sequential injection analysis (SIA) in spectrophotometric method[21]. The location of the end point using the present method is sharper and easier to define than that of the conductimetric method, which requires tedious extrapolation manipulation.

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Table 1. Determination of vitamin C by differential electrolytic potentiometric titrations compared with the official method

	Proposed method		Official method[3]	
Sample	Amt. taken (mg)	Recovery (%)[a]	Amt. taken (mg)	Recovery (%)[a]
Pure vitamin C		100.61	100	99.07
		99.33	150	101.87
		99.54	200	99.47
		101.03		
		101.99		
		100.80		
		100.00		
Mean ± S.D.[b]		100.47 ± 0.86		100.14 ± 1.24
t			0.22 (2.447)	
F			2.11 (19.3)	
Redoxon tablets	0.1	100.40	100	100.33
(1 g VitC/tab.)[c]	0.4	101.15	150	100.40
	1.0	99.20	200	101.26
Mean ± S.D.		100.25 ± 0.80		100.66 ± 0.42
t			0.788 (3.182)	
F			3.58 (19.0)	
Sedergine UPSA tablets	0.1	99.85	100	100.73
(200 mgVitC/tab.)[d]	0.4	99.35	150	101.00
Mean ± S.D.	1.0	100.40	200	100.13
t		99.87 ± 0.43		100.62 ± 0.36
F			2.315 (3.182)	
			1.39 (19.0)	
Dentake capsules	0.1	99.35	100	100.40
(150 mg Vit.C/tab.)[e]	0.4	100.95	150	99.35
	1.0	100.85	200	100.67
Mean ± S.D.		100.38 ± 0.73		100.14 ± 0.57
t				
F			0.452 (3.182)	
			1.65 (19.0)	
Orange juice	0.40	99.79	43	100.77
(43 mg VitC /100 mL)[f]	0.86	100.28	50	98.31
	1.50	98.81	70	100.23
Mean ± S.D.		99.63 ± 0.61		99.77 ± 1.06
t				
F			0.228 (3.182)	
			2.98 (19.0)	

[a]Average of three determinations.

[b]Mean ± standard deviation.

[c]Redoxon (Orange) vitamin C, Roche, Basel, Switzerland.

[d]Sedergine UPSA, Rueil-Malmaison, France.

[e]Dentake, Eisai Co. Ltd., Japan.

[f]Orange juice, Zain, S.A.O.G., Oman.

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