

Voltammetric Behavior of Menadione in Surfactant Media and Its Determination in Sodium Dodecyl Sulfate Surfactant System

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Cyclic voltammograms at the carbon paste electrode were recorded for menadione or vitamin K_3 dissolved in aqueous surfactant solutions above their critical micellization concentrations. The reduction and oxidation potentials of the vitamin were found to be different in different surfactants and were found also to vary with change in the surfactant concentration. Differential pulse voltammetric technique was utilized for the determination of the vitamin in the above surfactant systems. The limit of detection and the linear range varied in different surfactants, the lowest being in the sodium dodecyl sulfate surfactant systems. Similarly, cyclic voltammograms were recorded for ascorbic acid and the effect of various surfactants on its oxidation peak was also studied. Simultaneous determination of menadione, ascorbic acid, and riboflavin was attempted. Synthetically prepared samples were analyzed and gave satisfactory results.

Vitamin K represents a class of substances which contain the 2-methyl-1,4-naphthoquinone moiety and are characterized by their antihemorrhagic properties, i.e. they have long been recognized as essential constituents for blood coagulation and, owing to the reversible redox character of quinones, as electron mediators in the respiratory processes of the cells.[1] The K group of vitamers is typically found in green leafy vegetables such as cabbage, broccoli, cauliflower, and spinach; additionally, animal sources such as liver and eggs are also good sources of the vitamin. The K vitamins dissolve readily in most of the organic solvents like ether, petroleum ether, benzene, hexane, acetone, and butane and are sparingly soluble in methanol and ethanol; however, they are completely insoluble in water.[2] Menadione is the synthetic form of the vitamers. The quinonoid ring common to these vitamins is responsible for their physiological activity. This is shown by the fact that this synthetic compound is more potent on a molar basis than the natural vitamers are.

The electrochemical activity of these compounds, mainly the polarographic reduction of their quinone structure, is well known.[3,4] From an analytical point of view, the reversible two-electron transfer allows direct current and differential pulse polarographic determination of these vitamins in the 10^{-6} M to 10^{-7} M range.[5] The nature of the electrochemical reduction process for vitamin K_3 has been investigated by Patriarche and Lingane using direct current polarography and cyclic voltammetry at the HMDE; the supporting electrolyte consisted of phosphate or acetate buffers, containing 3–10% methanol. Milligram levels of the vitamin could be determined by a microcoulometric method of determination with electrogenerated Ce(IV) ion.[6] Later, Takamura and, Hayakawa[7] carried out cyclic voltammetric studies on the same vitamin in 70% methanolic acetate buffer at pH 4.8 and reported that the reduction was diffusion-controlled. Electrochemical reactions occurring for menadione at a platinum electrode were investigated by Cauquis and Marbach[8] in acetonitrile containing 0.1 M tetraethylammonium perchlorate. Square wave adsorptive stripping voltammetry of menadione at the SMDE dissolved in 20%(v/v) methanol–water mixture containing 0.3 M perchloric acid as the supporting electrolyte gave a detection limit of 1.3 $\times 10^{-10}$ M with 300 s accumulation time.[9] The most common colorimetric method for identifying menadione is to form a hydrazone with 2,4-dinitrophenylhydrazine. The resulting blue-green color is detected in an alkaline medium at 635 nm.[10]

Surfactant ions or molecules in aqueous solutions above a certain concentration form aggregates called micelles, which possess hydrocarbon-like interiors and polar surfaces. Much of the interest in micelles relates to the phenomenon of solubilization, whereby water-insoluble substances are dispersed in a medium, which is overall, an aqueous one.[11,12] When this vitamin is administered into the human body, the surrounding environment inevitably contains a major portion of the natural element water; it is thus important to understand the redox behavior of this vitamin in a completely aqueous system. In the present work, we have attempted to study the voltammetric behavior of vitamin K_3 dissolved in a completely aqueous environment with the help of certain ionic surfactants and a non-ionic surfactant viz, cetyltrimethylammonium bromide (CTAB), cetylpyridinium chloride (CPC), sodium dodecyl sulfate (SDS), and Triton X 100 (TX 100). Quantitative estimation of the vitamin in the above media was carried out by the differential pulse voltammetric (DPV) technique. Simultaneous analysis of the vitamins, menadione, ascorbic acid, and riboflavin has been taken up in the SDS media, as this surfactant provided the best separation of the peak potential values of the three vitamins.

Experimental

Chemicals and Reagents. All chemicals used were of analytical grade. Double-distilled, deionised water was used for preparation of all solutions. All the voltammetric studies were carried out in Britton Robinson (BR) buffer of pH 1.5 at 25 ± 0.2 °C.

Apparatus. The voltammetric system used for the studies was EG & G Princeton Applied Research 264A potentiostat with model 303A electrode assembly and X–Y chart recorder RE0089. The carbon paste electrodes were prepared as before.[13] The system was used in conjunction with a saturated calomel reference electrode and a platinum counter electrode.

Procedure. Cyclic voltammograms were recorded at different scan rates for a solution containing menadione (2×10^{-4} M) dissolved in 0.1 M CPC containing BR buffer at pH 1.5 as the supporting electrolyte. The surfactant concentration was then increased in the range 0.15–0.30 M and voltammograms were again recorded. The same procedure was followed to study the effect of other surfactants viz., CTAB, SDS, and TX 100. Cyclic voltammograms for ascorbic acid (3×10^{-3} M) and riboflavin (3×10^{-4} M) were also recorded in 0.1 M of all the above surfactants.

Differential pulse voltammetry (DPV) was utilized for the quantification of menadione in all the above media. The surface of the electrode was periodically renewed by pressing out a small amount of the paste, scraping off the excess, and polishing the tip on a zero grade polishing paper until the surface had a shiny appearance. Between successive runs, the solutions were purged with dry nitrogen for two minutes. DPV was also used for the quantification of ascorbic acid and riboflavin in the SDS system.

Simultaneous determination of menadione, ascorbic acid, and riboflavin was then taken up. Synthetic samples having compositions of the three vitamins viz., menadione:ascorbic acid:riboflavin in the ratios 15:76:10, 27:139:14, 46:236:19, and 71:408:26 μg cm^{-3} were prepared and their differential pulse voltammograms recorded.

Results and Discussion

Vitamin K_3 or menadione is a fat-soluble vitamin i.e. it comes under the class of vitamins which are completely insoluble in water. The vitamin is soluble in nonaqueous solvents and also in nonaqueous–aqueous solvent mixtures such as methanol–water, ethanol–water, acetonitrile–water, and dimethyl sulfoxide–water. However, in the presence of 0.1 M of certain surfactants viz., CPC, CTAB, SDS, and TX 100, the otherwise water insoluble vitamin is easily solubilized in what is essentially an aqueous matrix. Micellization of the surfactant monomers is a prerequisite for solubilization. The concentration of the surfactants has therefore been kept well above their critical micellization concentration (CMC) for complete dissolution of the vitamin (CMC's of SDS, CPC, CTAB and TX 100 are 8.1×10^{-3}, 9.0×10^{-4}, 9.2×10^{-4}, and 3.3×10^{-4} respectively). The reason why substances that are normally insoluble in water (or slightly soluble) may be solubilized in a micellar aqueous solution is that the interior of the micelle, which is assumed to be fluid-like, acts as a hydrophobic environment in which the hydrophobic molecule is easily dissolved.[14]

Cyclic voltammograms recorded for menadione (2×10^{-4} M) in BR buffer at pH 1.5 containing 0.1 M CPC at scan rate of 100 mV s^{-1} showed one peak each in both the forward and reverse scans. This is consistent with a two-electron reduction ($Ep_c = 0.16$) to produce the corresponding hydroquinone on the cathodic scan and re-oxidation of the hydroquinone ($Ep_a = 0.46$) on the anodic scan. At higher concentrations of the surfactant CPC, the reduction peak potentials shifted to more negative values and the oxidation peak potentials shifted to more positive values, indicating deviation from reversibility of the quinone–hydroquinone couple. This is because of an increase in the size of the micelles, which is caused either because of an increase in the surfactant concentration or because of incorporation of the solubilizate in the micelles, thus leading to an increase in the average number of surfactant molecules in the micelles.[15] The increased micellar size tends to increase the residence time of the analyte in the micelle,[16] causing both the reduced and oxidised species to remain in the micelle for a longer time, thus making them unavailable for reduction or oxidation at the same potentials as before. The consequence is a delay in the redox processes of the quinone–hydroquinone system as the surfactant concentration goes up. Also, both the reduction peak current (Ip_c) and oxidation peak current (Ip_a) steadily decreased with increasing CPC concentration. This is again because, as the micellar size increases, the micelles become heavier and bulkier and thus their transport to the electrode surface becomes slower. Since the vitamin molecules are embedded inside the micelles, they must travel along with the micelles, thus leading to decreased peak currents as the surfactant concentration goes up. Therefore there is a decrease in the diffusion coefficient of the analyte as a result of the decreased diffusion coefficient of the micelles. Kirchoff et al.[17] reported similar observations in their studies on rhenium and technetium complexes in micellar media. Similar effects have been observed with menadione dissolved in CTAB and the anionic surfactant SDS. However, in the SDS media, with increase in concentration of the surfactant, the change in the reduction and oxidation potentials is not as much compared to that in cationic surfactants and the peak currents are observed to be much higher. This could be mainly because cationic micelles are able to solubilize more of a given substrate than are anionic and nonionic micelles. The reason for this is that the cationic systems have a larger volume of hydrophobic character with which to accept an organic substrate, due to their softer head groups,[18] which allow a smaller interhead group separation.[19] Hence the organic substrate is embedded deeper into the hydrophobic core in the cationic micelles, whereas in the case of anionic micelles of SDS, the vitamin may be present in the palisade layer. This results in higher reduction and oxidation potentials in cationic micelles of CPC and CTAB and lower peak currents as compared to the anionic micelles of SDS. In the case of nonionic surfactant TX 100, the reduction potentials are much lower than those in either the cationic or the anionic surfactants. TX 100 molecules have electron-donating poly(oxyethylene) headgroups, which facilitate the reduction process of menadione. The oxidation potential, however, is almost comparable with that in SDS. Increase in surfactant concentration further reduces the reduction potential very slightly, but has no effect on the oxidation potential. In each of the surfactants, voltammograms were recorded at scan rates of 20 mV s^{-1}, 50 mV s^{-1}, 100 mV s^{-1}, and 200 mV s^{-1}. The plots of current (I_p) vs square root of scan rate ($v^{1/2}$) were found to be linear in all the media, indicating the diffusion-controlled nature of the redox reaction. Table 1 shows the effect on Ep_c, Ep_a, Ip_c, and Ip_a for menadione in different concentrations of different surfactants.

Cyclic voltammograms were also recorded for riboflavin (vitamin B_2) and ascorbic acid (vitamin C) in 0.1 M of each of

Table 1. Effect on the Peak Potentials and Peak Currents of Menadione (2×10^{-4} M), in Different Concentrations of Different Surfactants as Obtained by Cyclic Voltammetry

Concentration of surfactant M	E_{pc} V	I_{pc} μA	E_{pa} V	I_{pa} μA	E_{pc} V	I_{pc} μA	E_{pa} V	I_{pa} μA
	SDS				TX 100			
0.10	0.12	12.0	0.22	15.0	0.10	10.3	0.20	13.0
0.15	0.10	11.2	0.24	14.3	0.08	10.3	0.19	13.0
0.20	0.08	11.0	0.26	14.0	0.06	10.0	0.19	13.0
0.25	0.05	10.8	0.26	13.8	0.05	10.3	0.20	13.0
0.30	0.02	10.5	0.28	13.5	0.05	10.0	0.20	13.3
	CPC				CTAB			
0.10	0.16	9.0	0.46	12.0	0.15	9.8	0.44	12.8
0.15	−0.08	7.2	0.48	10.0	−0.05	8.3	0.45	11.3
0.20	−0.14	6.5	0.50	9.5	−0.10	8.0	0.45	11.0
0.25	−0.20	6.3	0.53	9.3	−0.15	7.8	0.50	10.8
0.30	−0.22	6.0	0.55	9.0	−0.15	7.8	0.50	10.8

Table 2. Effect On the Peak Potentials and Peak Currents of Ascorbic Acid (3×10^{-3} M) and Riboflavin (3×10^{-4} M), in BR Buffer at pH 1.5 only and BR Buffer at pH 1.5 Containing 0.1 M of the Surfactant

Medium	Riboflavin				Ascorbic acid	
	E_{pc} V	I_{pc} μA	E_{pa} V	I_{pa} μA	E_p V	I_p μA
BR buffer pH 1.5	−0.02	8.0	0.02	9.0	0.60	8.5
SDS	−0.02	18.2	0.02	19.6	0.60	8.3
TX 100	−0.02	7.8	0.02	9.0	1.00	6.0
CPC	−0.09	7.4	−0.02	9.1	0.75	5.9
CTAB	−0.12	6.2	−0.03	8.8	0.63	6.2

the above surfactants. Table 2 shows the values of the peak currents and peak potentials of riboflavin and ascorbic acid in BR buffer at pH 1.5 only and in BR buffer at pH 1.5 containing 0.1 M of the surfactants. Voltammograms recorded at different scan rates showed diffusion-controlled behavior. A comparison of the oxidation peak potentials of the three vitamins in 0.1 M SDS shows the difference in the E_{pa} values to be 200 mV between vitamins B_2 and K_3 and 380 mV between the vitamins K_3 and C. In 0.1 M CPC the difference in E_{pa} values is 480 mV between vitamins B_2 and K_3 and 290 mV between vitamins K_3 and C. In 0.1 M CTAB the difference is 470 mV between vitamins B_2 and K_3 but only 190 mV between vitamins K_3 and C and lastly in 0.1 M TX 100 the difference in E_{pa} values is only 170 mV between vitamins B_2 and K_3 and 800 mV between vitamins K_3 and C. Thus it is seen that the SDS and the CPC systems offer the best resolution in the oxidation peak potentials of all the three vitamins. Figure 1 shows the cyclic voltammograms for the mixture of menadione, ascorbic acid and riboflavin in 0.1 M SDS.

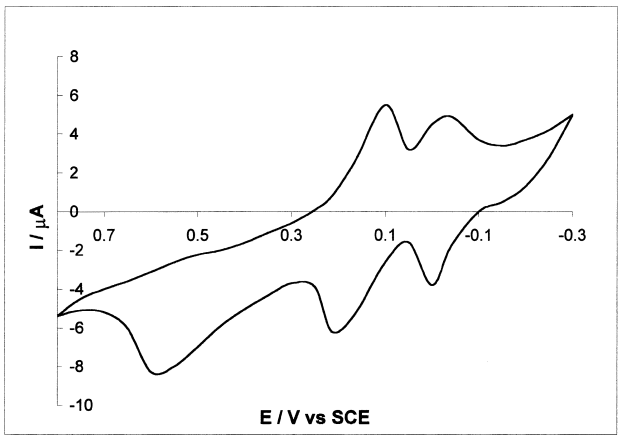

Fig. 1. Cyclic voltammograms for the simultaneous determination of menadione (3×10^{-4} M), ascorbic acid (3×10^{-3} M), and riboflavin (3×10^{-4} M) in a synthetically prepared sample at a scan rate of 100 mV s^{-1} in 0.1 M SDS.

Differential pulse voltammetry was used for the quantification of vitamin K_3 in all the above media. The limit of detection was obtained from the lowest concentration that gave a distinctly detectable and reproducible peak after performing the experiment seven times. Both the limit of detection and the linear concentration range observed were different in each system, as can be seen from Table 3. The lowest limit of detection, 0.3 μg cm^{-3} (RSD = 4.0%), was observed in the SDS mi-

Table 3. Linear Concentration Range and Limit of Detection Observed for Vitamin K_3 in Each of the Surfactant Systems by DPV at Scan Rate 20 mV s^{-1} and Pulse Height 50 mV

Surfactant	Detection limit	RSD	Linear conc. range	Coefficient of correlation
	μg cm^{-3}	%	μg cm^{-3}	
SDS	0.3	4.0	0.8–200	0.9930
TX 100	0.6	4.2	1.0–200	0.9948
CPC	1.2	4.0	1.8–200	0.9926
CTAB	0.8	4.3	1.5–200	0.9912

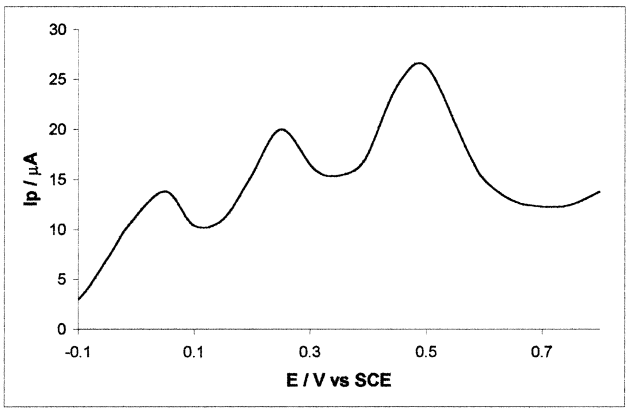

Fig. 2. Simultaneous determination of menadione:ascorbic acid:riboflavin in the ratios 71 μg cm^{-3}:408 μg cm^{-3}:26 μg cm^{-3} in a synthetically prepared sample by DPV at a scan rate of 20 mV s^{-1} and pulse height 50 mV in 0.1 M SDS.

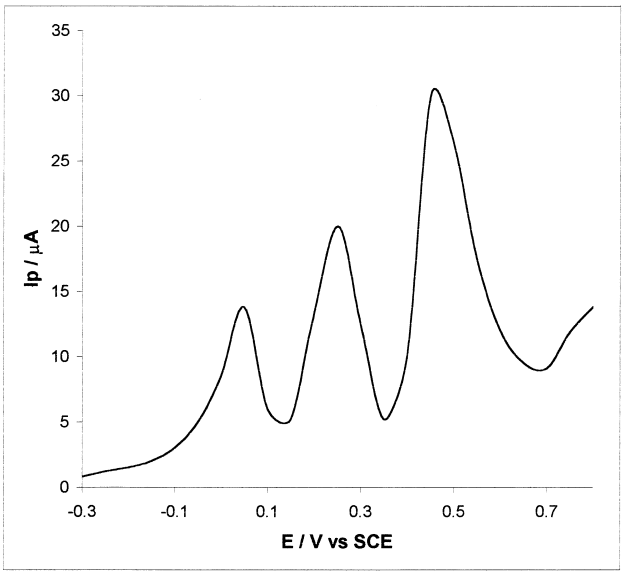

Fig. 3. Simultaneous determination of menadione:ascorbic acid:riboflavin in the ratios 71 μg cm^{-3}:408 μg cm^{-3}:26 μg cm^{-3} in a synthetically prepared sample by DPV at a scan rate of 5 mV s^{-1} and pulse height 100 mV in 0.1 M SDS.

cellar system. The linear working range was observed to be between 0.8 μg cm^{-3} and 200 μg cm^{-3} (coefficient of correlation = 0.9930), at a scan rate of 20 mV s^{-1} and a pulse amplitude of 50 mV. By lowering the scan rate to 10 mV s^{-1} and 5mV s^{-1} and increasing the pulse amplitude, sharper peaks were obtained and a detection limit of 0.07 μg cm^{-3} for menadione was possible. Further studies were thus carried out in the above surfactant system.

In the same medium, linear working ranges from 50 μg cm^{-3} to 500 μg cm^{-3} of ascorbic acid (coefficient of correlation = 0.9927), and from 5 μg cm^{-3} to 50 μg cm^{-3} of riboflavin (coefficient of correlation = 0.9987), at a scan rate of 20 mV s^{-1} and a pulse amplitude of 50 mV were observed.

Simultaneous determination of menadione, ascorbic acid, and riboflavin was then carried out. Figure 2 shows the differential pulse voltammograms for the simultaneous determination of the three vitamins at a scan rate of 20 mV s^{-1} and a pulse amplitude of 50 mV. The peaks though visible, seem to merge with each other. For better resolution, the scan rate was dropped to 10 mV s^{-1}. Figure 3 shows that an increase in pulse amplitude to 100 mV and a further drop in scan rate to 5 mV s^{-1}, gave the best resolution. Synthetic samples of different compositions of the two vitamins were analyzed and gave good results. Table 4 compares the actual and observed contents obtained for both the vitamins in the mixtures of different proportions.

Conclusion

It has been observed that the presence of surfactants causes the dissolution of menadione, which is essentially a fat-soluble vitamin, in a completely aqueous system. This could be due to the incorporation of the vitamin in the micelles of the surfactants. Many active derivatives and homologues of menadione or the natural vitamins have been prepared to render them water-soluble; however, this has always led to a diminition or loss of biological potency. This may thus be avoided by making the vitamin water-soluble with the help of surfactants, especially for the formulation of aqueous injections. The detection limits reported in the present work are almost comparable or are even lower than those observed by other more commonly employed methods for the analysis of the vitamin, such as colorimetry and spectrophotometry. Simultaneous determination of menadione, ascorbic acid, and riboflavin has been made possible mainly due to the shifts caused in the oxidation peak potential values as an effect of the surfactant. This otherwise may not have been possible due to an overlap in the peak potentials.

Table 4. Accuracy and Precision of the Method for Simultaneous Determination of Menadione, Ascorbic Acid, and Riboflavin in BR Buffer at pH 1.5 Containing 0.1 M SDS

Synthetic sample	Observed Content		
Menadione : Ascorbic acid : Riboflavin	Menadione	Ascorbic acid	Riboflavin
15 μg cm^{-3} : 76 μg cm^{-3} : 10 μg cm^{-3}	14.2 ± 1.2 ($n = 5$)	74.2 ± 1.8 ($n = 5$)	9.8 ± 0.8 ($n = 5$)
27 μg cm^{-3} : 139 μg cm^{-3} : 14 μg cm^{-3}	25.8 ± 1.5 ($n = 5$)	135.8 ± 1.8 ($n = 5$)	12.2 ± 0.8 ($n = 5$)
46 μg cm^{-3} : 236 μg cm^{-3} : 19 μg cm^{-3}	42.8 ± 0.9 ($n = 5$)	240.2 ± 1.6 ($n = 5$)	16.2 ± 0.9 ($n = 5$)
71 μg cm^{-3} : 408 μg cm^{-3} : 26 μg cm^{-3}	69.0 ± 1.2 ($n = 5$)	401.0 ± 1.2 ($n = 5$)	22.1 ± 1.2 ($n = 5$)

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