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Dedicated to Professor Victor-Emanuel Sahini on the occasion of his 85th anniversary

CYCLIC VOLTAMMETRY OF QUERCETIN IN THE PRESENCE OF SODIUM DODECYL SULFATE

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The critical micelle concentration (cmc) of sodium dodecyl sulfate (SDS) is obtained using cyclic voltammetry (CV) technique and quercetin as electroactive probe at three different pH values. The quercetin interacts with micelle aggregate in a specific mode and its concentration in the bulk electrolyte solution is modified when micelles are formed. The anodic peak currents depend in a sigmoidal feature upon the concentration of the SDS, the inflexion point of the sigmoidal fit being used to determine the cmc. A peak current jump, which depends upon the pH, could be measured on the sigmoidal curve. The reversibility itself of the electrode reaction of quercetin experiences a passage from reversible to quasireversible behavior depending on the pH increase. A technique of titration (standard addition methods) was used. The titrated solution and the titrating solution contain the same concentration of quercetin and have the same pH, the SDS being solved in titrating solution. At each addition the solution was intensively stirred and three cyclic voltammograms at different scan rates were recorded. Three groups of cyclic voltammograms could be identified according to the three regions encountered: premicellar, micellar or postmicellar. A weak anodic shift of the anodic peak potential at each investigated pH results in comparison to the position of the anodic peak obtained in the absence of the SDS.

INTRODUCTION

Flavonoids are a large family of polyphenolic compounds, synthesized by plants, having a common chemical structure with 15 carbon atoms. The flavonoids consist of 6 major subgroups: chalcone, flavone, flavonol, flavanone, anthocyanins and isoflavonoids. Flavonoids are becoming very popular because they have many health promoting effects. Their biological activities is reflected in direct antioxidant properties, flavonoids being effective scavengers of free radicals, they can chelate (bind) metal ions, modulate of cell-signaling pathways. Flavonoids could help prevent cancer by: stimulating phase II detoxification enzyme activity, preserving normal cell cycle regulation, inhibiting proliferation and inducing apoptosis, inhibiting tumor invasion and angiogenesis, decreasing inflammation.[1-6]

One of the most common plant-derived flavonoids that can be found in nature is quercetin (3,5,7,3',4'-pentahydroxyflavone, IUPAC name: 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4*H*-chromen-4-one, Fig. 1). Its structure consists of two benzene rings (A and B) which are joined together with a three carbon chain. One of the carbons of the short chain is always connected to a carbon of one of the benzene rings, either directly or through an oxygen bridge, thereby forming a third middle ring (ring C). Quercetin belongs to the flavonoid family of compounds and possesses a variety of biological and biochemical effects, including cardiovascular protection, anti-cancer and anti-inflammation activity.[7-12]

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The polyphenolic structure of quercetin is very sensitive to changes produced in the environment in which it exists. These modifications would affect the hydrophobicity, solubility and electrochemical properties of quercetin, which could eventually lead to the change of its antioxidant activity. There is little information concerning the influence of the surroundings on quercetin structure. Therefore, a study of interaction between flavonoids and molecular organized assemblies, as micelles, formed by different surfactants could be very important. The molecular organized assembly has structure similarity to the cell and protein in the life systems and rich diversity in the microstructures.[13,14]

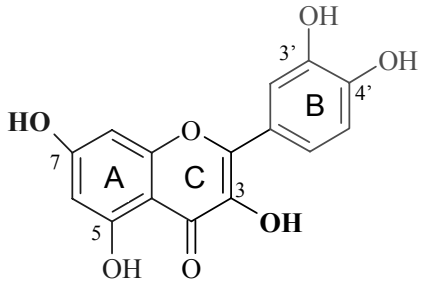

Fig. 1 – The structure of quercetin.

In spite of the attention paid to the interaction of the Q with organized surfactant aggregates,[15,16] this paper aims to complete the study already done in order to obtain the cmc by using a different approach (some kind of titration procedure) which allows to measure the current peak as a function of the SDS concentration.

EXPERIMENTAL

Apparatus: Electrochemical experiments were carried out using the potentiostat-galvanostat system AutoLab PGStat 12, controlled by General Purpose Electrochemical System (GPES) electrochemical interface for Windows (version 4.9.007). Three electrodes in one-compartment cell (10 mL) were used in all experiments. Glassy carbon electrode (GCE) served as a working substrate electrode. All potentials were measured and given referred to $Ag/AgCl/KCl\,(3\ M)$ used as reference electrode. The counter electrode was a platinum electrode disk-shaped. The GCE and platinum electrode surfaces were polished with alumina slurry on a polishing pad, washed with distilled water and sonicated for 1 minute and 3 minutes, respectively, in doubly distilled water.

Chemicals: All chemicals were reagent grade. Quercetin (Q) (Roth), sodium dodecyl sulfate (SDS) (Carlo Erba), methanol (Fluka), acetic acid (Sigma), and sodium hydroxide (Sigma) were used as received.

Measurements: Quercetin was solved in methanol to obtain a 0.2 mM solution, as stock solution. Three different acetic acid–sodium acetate buffer solutions (ABS), were prepared in distilled water at pH 4.6, 5.0, and 5.4. By mixing 1 mL of 0.2 mM Q in methanol, in turn, with 9 mL of ABS at a given pH, three titrated solution were obtained; these solutions were used as electrolyte solutions in the electrochemical cell. Three solutions containing 0.1 M SDS in ABS of pH 4.6, 5.0, and 5.4, respectively were prepared. Three titrating solutions were obtained by mixing 9 mL SDS in buffer solutions with 1 mL of 0.2 mM Q in methanol. Three parallel sets of experiments were performed, by adding portions of 0.1 mL of each titrating solution, under intense stirring conditions lasting 2 minutes, in 10 mL titrated solution in electrochemical cell, both solutions having the same pH. Then the solution was let to become quiet and CV measurements were performed from 0.1 to 0.5 V for pH 4.6 and 5.0 and from 0.0 to 0.5 V for pH 5.4, respectively at three scan rates, 20, 50, and 100 mV/s. All measurements were carried out at room temperature.

RESULTS AND DISCUSSION

Cyclic voltammograms of quercetin in methanol/ABS solution at pH 5, in the potential range from 0.1 to 0.5 V, at different scan rates from 10 to 100 mV/s, are presented in Fig. 2. The same kind of studies was performed for the two titrated solutions at other pH values, 4.6 and 5.4, respectively. In all cases, a pair of peaks appears. The value of half-peak potentials and peak-to-peak separation are listed in Table 1.

Table 1

The values of $E_{1/2}$, ΔE_p, and $\frac{I_{pa}}{I_{pc}}$, for 10 mV/s and 100 mV/s, respectively, at the three pH used

pH	**4.6**			**5.0**			**5.4**		
	$E_{1/2}$ (V)	ΔE_p (V)	$\frac{-I_{pa}}{I_{pc}}$	$E_{1/2}$ (V)	ΔE_p (V)	$\frac{-I_{pa}}{I_{pc}}$	$E_{1/2}$ (V)	ΔE_p (V)	$\frac{-I_{pa}}{I_{pc}}$
10 mV/s	0.352	0.068	1.14	0.331	0.083	1.13	0.325	0.079	1.13
100 mV/s	0.359	0.088	1.12	0.337	0.094	1.01	0.345	0.115	1.10

The logarithmic plot of anodic peak intensity (I_{pa}) vs. scan rate (v) is linear in the investigated scan rate range and leads to slopes near 0.5 (0.66 for pH 4.6, 0.59 for pH 5, and 0.57 for pH 5.4, respectively) showing a consistent diffusional behavior of the redox species with a small contribution of absorbed electroactive species, contrary to the result obtained at GCE,[15] where it is stated that a strong adsorption occurs. In addition, quercetin is weakly absorbed on the electrode surface, the anodic peak current being in a small extent increased (as can be seen from peak current ratio in Table 1, at each pH), both surface and diffusional electrode reactions occurring at the same anodic peak potential. The peak-to-peak separation is also given in Table 1.

The addition of SDS modifies the intensity of anodic (direct) peak current, as can be seen in Fig. 3, where I_{pa} vs. c_{SDS} (where c_{SDS} is the concentration of SDS in the titrated solution) was plotted.

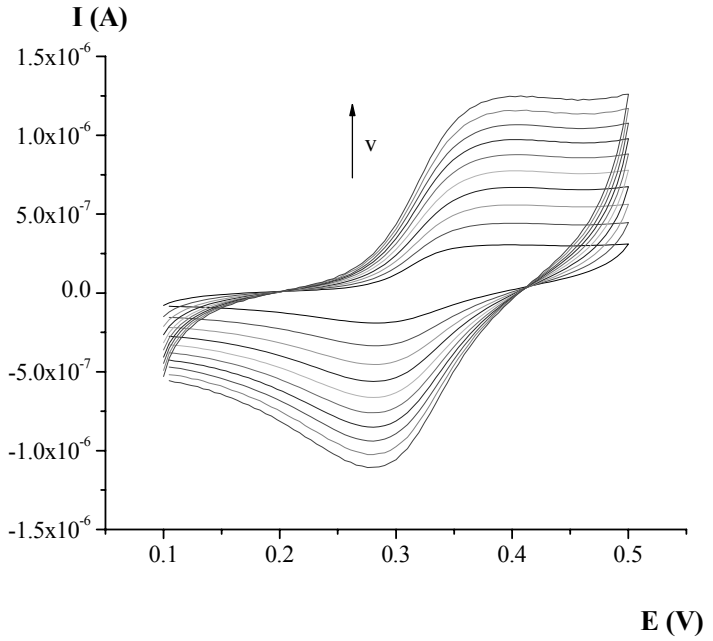

Fig. 2 – Cyclic voltammograms of quercetin (2 x 10^{-5} mol/L) in ABS with pH = 5.0 at scan rates from 10 to 100 mV/s.

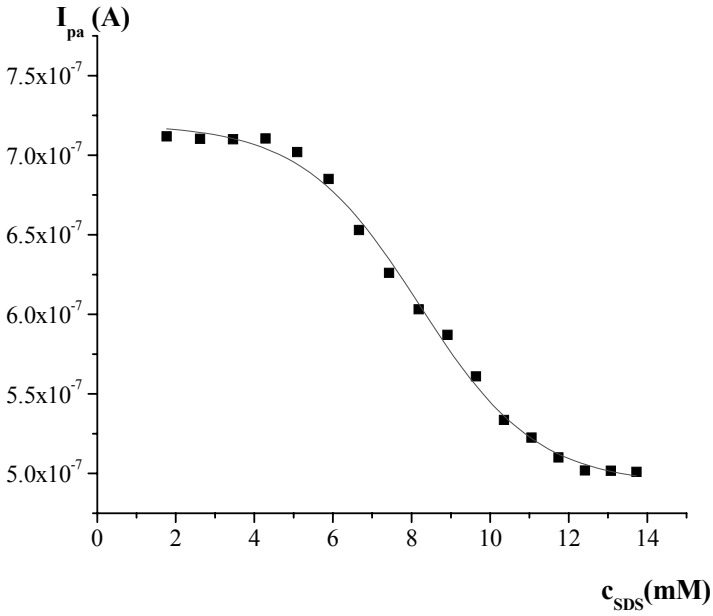

Fig. 3 – The sigmoidal dependence of I_{pa} vs. c_{SDS} at pH being 5.0. Scan rate: 50 mV/s.

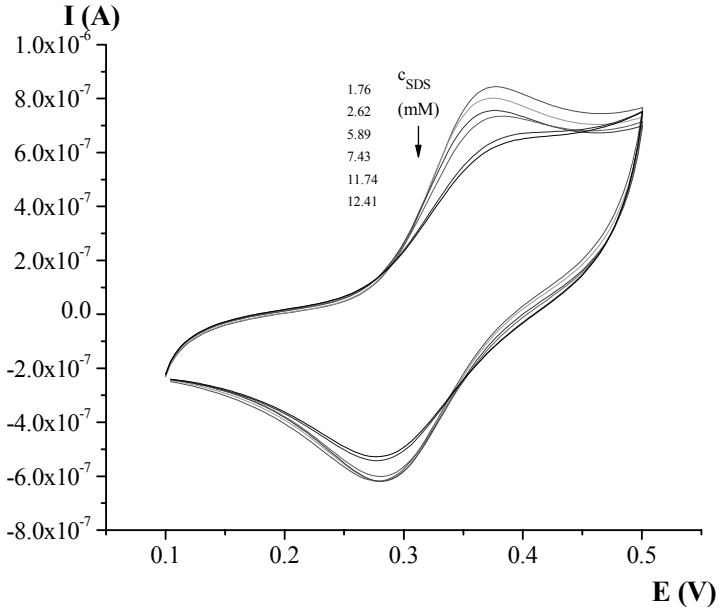

Fig. 4 – Cyclic voltammograms of quercetin (2 x 10^{-5} M) in SDS/ABS systems having different concentrations of SDS at pH being 5.0. Scan rate: 50 mV/s.

By fitting the experimental points with a sigmoidal procedure, the cmc can be determined as the inflexion point of the curve. The peak current decrease is very clear in the middle region corresponding to micelle formation.

Three regions can be identified on the curve: i) one before the cmc (for concentration of SDS lower then 3.46 mM), which shows a more or less constant peak current, ii) other situated on the steep decreasing part (for concentration of SDS in the range of 3.45 to 10.35 mM), and iii) one after the cmc (for concentration of SDS higher then 10.35 mM), which shows again a more or less constant peak current.

This behavior can also be observed in Fig. 4, where two cyclic voltammograms belonging to each region are considered. Three different groups of cyclic voltammograms appear for $c_{SDS} < cmc$, for $c_{SDS} \approx cmc$, and for $c_{SDS} > cmc$. As can be seen, in the premicellar and postmicellar regions the peak currents are almost constant or decay very slowly, while in the micelles formation region rapid decrease of them is recorded.

The voltammograms show a small loss of the reversibility even at a very low scan rate at each pH used and even in the absence of SDS (see peak-to-peak separation in Table 1). In addition, the anodic peak potential shifts in the anodic direction very little for pH 4.6 (only 7 mV), and pH 5.0 (only 6 mV), but with 20 mV for pH 5.4. As concerns the cathodic peak potentials, they remain almost constant: 318 mV for pH 4.6, 290 mV for pH 5.0, and 285 mV for pH 5.4. As concern the peak current ratios, they are in the domain 1.14-1.12 for pH 4.6, and 1.13-1.10 for pH 5.4, but 1.13-1.01 for pH 5. The same behavior could be seen even in the premicellar region which can be attributed to the manifestation of very weak interactions between the quercetin and surfactant molecules by the probable association of the electroactive species with the hydrophobic environment offered by continuous increase of the surfactant concentration until the micellization process is accomplished. In the postmicellar region the same behavior could be encountered, perhaps due to the increase of the number of micelles, and, as a consequence, due to a slight decrease of the free concentration of quercetin.

The influence of the pH on the cyclic voltammograms shape, the value of the peak currents and of the peak current jumps around the cmc can be observed in Figs. 5 and 6 and in Table 2. Increasing the pH the cyclic voltammograms lose reversibility, their appearance changes from the reversible to the quasireversible case, irrespective of the premicellar, jump or postmicellar region in which they are recorded. The half-wave potential is also shifted in the negative direction with increasing pH. Both anodic and cathodic peak currents decrease with increasing pH for the same scan rate used in CV experiments.

Table 2

The values of cmc and the current peak jumps from premicellar to postmicellar regions at different pH and different scan rates used in the titration process

pH	**4.6**			**5.0**			**5.4**		
v (mV/s)	**20**	**50**	**100**	**20**	**50**	**100**	**20**	**50**	**100**
cmc (mM)	7.35	6.49	6.44	6.70	8.32	7.79	7.73	7.68	7.53
mean cmc (mM)	6.76			7.60			7.65		
I_{jump} (nA)	42.67	84.95	190.30	93.42	230.23	425.66	79.70	104.82	168.53

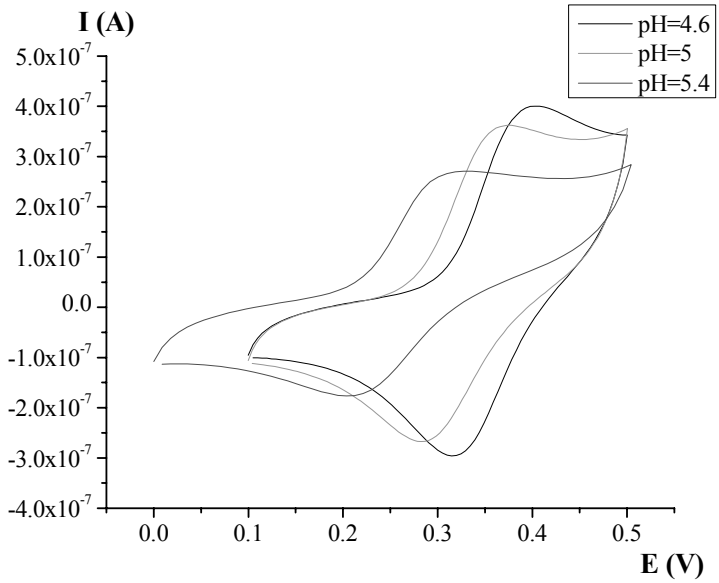

Fig. 5 – The cyclic voltammograms for quercetin (2 x 10^{-5} M) + SDS (2.62 mM) system at different pH values: 4.6, 5.0, 5.4. Scan rate: 20 mV/s.

Fig. 5 shows how the cyclic voltammograms recorded for quercetin in the presence of 1.76 mM SDS change with pH. This happens for any concentration of SDS, their shape changes similarly with pH changing from 4.6, then to 5.0, and finally to 5.4. In addition, the anodic peak potential generated by anodic oxidation of quercetin moves towards less anodic electrode potential while the pH increases. Correspondingly, the anodic peak current decreases when the pH increases. Both above mentioned results support the idea that the oxidation of quercetin becomes increasingly slower while the pH becomes increasingly basic, at least in the pH range investigated.

The most plausible hypothesis is that the redox site of the quercetin is, in some extent, embedded somewhere in the micelle and the deelectronation process is somehow hindered in some degree in this special location. As the cathecol structured cycle in quercetin is involved in anodic oxidation (cathecol/o-benzoquinone-like electrode reaction),[17] it results that this cycle is hidden[15,16] in the micelle structure being less exposed to the deelectronation process. An argument for this assumption is the dipole moment orientation of the quercetin, from cycle B towards cycle A (Fig. 1). In this way the interaction of the positive pole of the dipole moment with the negative spherical surface of the micelle is favourable for such a lay-out/location/arrangement of the quercetin molecule in relation to the micelle. Another way to consider this interaction is given by the acid-base equilibrium which indicates that the most acidic hydroxyl group is phenolic OH in the position 7 (on the cycle A, also the OH in position 3 on cycle C).[18,19] So this cycle, namely A, is repelled by the negative spherical surface (formed by the polar heads of the surfactant) of the micelle. As a consequence, the quercetin molecule will interact by means of cycle B with the micelle, not by cycles A and C, which will be electrostatically rejected. The picture of this spatial arrangement is the following: the cycle B enters the superficial micelle while the cycle A flows outside the micelle being „solved" in the bulk solution. Besides this electrostatic interaction, the quercetin molecule and SDS aggregate can interact hydrophobically due to their own hydrophobic regions.

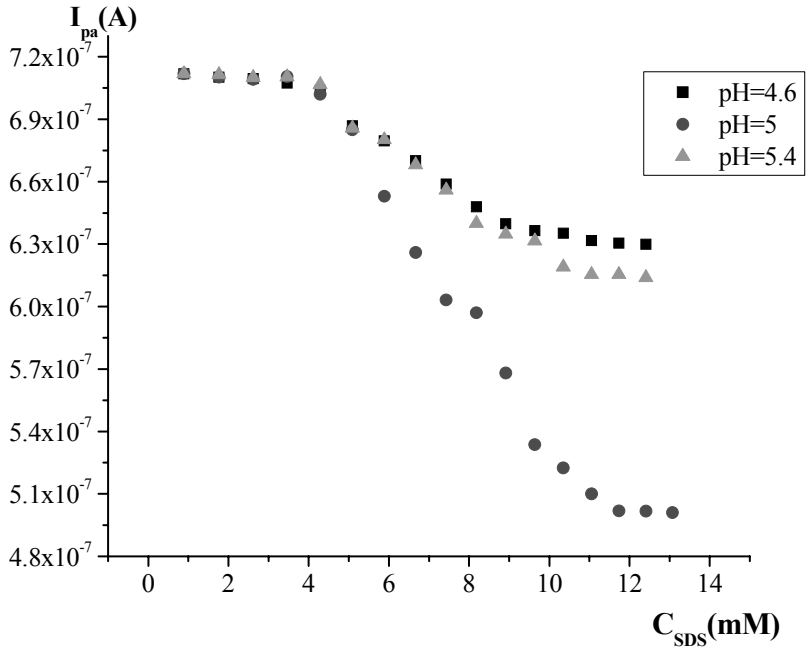

Fig. 6 – The sigmoidal dependence I_{pa} vs. c_{SDS} obtained at the titration of Q 2 x 10^{-5} mol/L in ABS with Q 2 x 10^{-5} mol/L, 0.1 M SDS in ABS at certain pH. Scan rate 50 mV/s.

In Fig. 6 the peak current jumps around the cmc for the three used pH, at a scan rate of 50 mV/s, are shown. All these values, also presented in Table 2, were determined after the sigmoidal fit of the experimental data. The largest jump is measured for pH 5.0 although the anodic peak current is largest at pH 4.6. The smallest peak current jumps are determined for pH 5.4

CONCLUSIONS

The cyclic voltammetry studies of 0.02 mM Q in methanol and ABS of different pH show a passage from reversible to quasireversible behavior of the electroactive quercetin as the pH increases. In the presence of SDS, the influence of pH on the shape of the cyclic voltammograms is quite similar irrespective of the group (premicellar, micellar or postmicellar region) to which they belong. By comparing the cyclic voltammograms obtained in the absence and in the presence of the micelles, it results a weak anodic shift of the anodic peak potential at each pH investigated. This displacement is determined by the formation of the micelles and by the interaction of the electroactive probe with the surfactant aggregates. This interaction sends the anodic reaction of quercetin to more anodic potential, so in the presence of SDS aggregates the electroactive quercetin experiences a harder anodic electrode reaction. From the sigmoidal fitting of the anodic peak current vs. the surfactant concentration, it is possible to determine, from the inflexion point, the cmc at each pH used and for each scan rate used in recording cyclic voltammograms. The peak current jumps are largest at pH 5 for each scan rate used then for pH 4.6, the smallest jumps correspond to pH 5.4.

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