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# Electrochemical study of quercetin–DNA interactions: Part I. Analysis in incubated solutions

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**Abstract**

The present study aims to investigate the quercetin–deoxyribonucleic acid (DNA) interaction occurring in bulk solution either electrochemically using differential pulse voltammetry or spectrophotometrically, in order to explain the possible DNA-damaging activity of quercetin. A very weak interaction between quercetin and DNA in solution was found to take place. However, since extensive quercetin-induced DNA damage via reaction with Cu(II) has been reported, an electrochemical study of the DNA–Cu(II)–quercetin system in solution was undertaken. The product of DNA interaction with quercetin–Cu(II) complex was observed. Damages to DNA were electrochemically recognized via the increasing of the anodic peaks corresponding to the oxidation of guanosine and adenosine bases and spectrophotometrically via increasing of the 260 nm adsorption band. It was also observed that dsDNA damage produced by the quercetin–Cu(II) complex occurred with time. Control experiments with different mixtures of Cu(II), quercetin, ssDNA, dsDNA or poly[A] were carried out in order to establish a possible mechanism of interaction between DNA and quercetin via Cu(II).


*Keywords:* DNA-electrochemical biosensors; Quercetin; Oxidation; Electrochemistry; Radical scavenging activity; Flavonoids

## 1. Introduction

Reactivity of deoxyribonucleic acid (DNA) and damage to DNA are important from both a chemical as well as a medical point of view; therefore, there is a lot of experimental evidence proving that DNA can be damaged by various physical and chemical factors [1–3]. Recently, a great interest in the role of reactive oxygen species (ROS) in damage to DNA has been taken in the field of mutagenesis. ROS produced in vivo react with DNA and its precursors modifying them, therefore, giving rise to the so-called oxidative stress. It is thought that the modification of DNA (DNA lesion) leads to formation of incorrect base pairs, changes in the genetic information, which induce mutagenesis and carcinogenesis. Therefore, in a health preventing perspective, there is a deep interest in identifying free radical scavengers or antioxidants that inhibit oxidative DNA damage. Owing to their polyphenolic nature, flavonoids, compounds found in rich abundance in all land plants, often exhibit strong antioxidant properties [4–6]. Initially, flavonoids were investigated as potential chemopreventive agents against certain carcinogens. Previous intake of a large quantity of flavonoid inhibited the incidence of ROS produced damages to DNA. In sharp contrast with the commonly accepted role, there is also considerable evidence that flavonoids themselves are mutagenic and have DNA damaging ability [5,6].

One striking example reported in the literature is that of quercetin, Scheme 1, which in presence of transition metals acts as a prooxidant and has mutagenic activity [7,8]. It was shown that some flavonoids are able to reduce transition metals, a process during which the highly oxidizing radical OH is formed and therefore it could damage DNA.

The effects of quercetin and other flavonoids that have similar structures on isolated DNA were examined using electrophoretic [9], spectrophotometrical [9,10], and fluorimetric [11] methods as well as HPLC [12] and voltammetric detection [10,13]. Several studies have shown that the *o*-dihydroxy structure in the ring B of quercetin is important for Cu(II) ions chelation [14–16]. There are evidences that the complex formed between quercetin and transition metals binds to DNA by intercalation [17,18]. However, the binding

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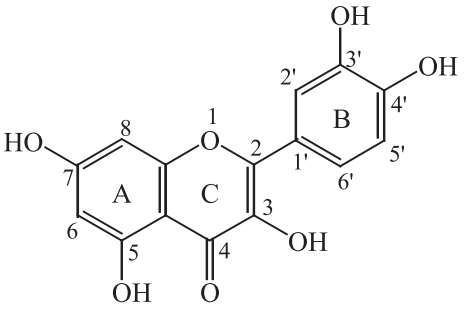


Scheme 1. Quercetin structure.

reaction occurs and these methods have given evidence that under some experimental conditions and in the presence of a high concentration of quercetin, strand breakages into plasmid DNA could occur [5] and on the other hand, the detection of 8-oxoguanine was possible [9].

In this context, the aim of the present paper is concerned with studying the interaction of quercetin with dsDNA using electrochemical and spectrophotometrical methods. Since extensive quercetin-induced DNA damage via reaction with Cu(II) has been reported, an electrochemical study of the DNA–Cu(II)–quercetin system was undertaken. The experimental results presented here will give evidence that quercetin can undergo oxidation in the presence of DNA double helix and a weak interaction between them was found to take place. On the other hand, the addition of Cu(II) ions leads to the formation of a new product and damage to DNA was detected via increasing signals of guanine and adenine bases. Nevertheless, following differences into the adsorption spectra, an increase of the adsorption band at 260 nm after DNA interaction with quercetin–Cu(II) complex was found.

## 2. Experimental

### 2.1. Substances and stock solutions

Quercetin, sodium salt calf thymus single stranded (ss) DNA, double stranded (ds)DNA, polyadenylic acid—poly [A], 8-oxoguanine from Sigma, and $CuSO_4$ obtained from Merck were used without further purification.

Stock solutions of 500 μM saturated quercetin, 1 mM $CuSO_4$, 100 μg $ml^{-1}$ ssDNA, dsDNA and poly[A] were prepared in pH 4.3, 0.1 M acetate buffer electrolyte and stored at −4 °C. All solutions were prepared using analytical grade reagents and purified water from a Millipore Milli-Q system (conductivity ≤0.1 μS $cm^{-1}$). All experiments were done in pH 4.3, 0.1 M acetate buffer at room temperature (25 ± 1 °C).

### 2.2. Apparatus, software and data treatment

All voltammetric measurements were carried out using a PGSTAT 10 Autolab running a GPES software version 4.9, Eco-Chemie, Utrecht, Netherlands. A glassy carbon working electrode (GCE) ($d$ = 1.5 mm), a platinum wire counter electrode and an Ag/AgCl (sat KCl) as reference were used in a 0.5 ml one-compartment electrochemical cell. During DNA–quercetin interaction, the solutions were continuously stirred. The experimental conditions for differential pulse voltammetry were: pulse amplitude 50 mV, pulse width 70 ms and scan rate 5 mV $s^{-1}$. All the voltammograms obtained were smoothed using Savitsky-Golay algorithm and base line corrected by the moving average method (peak width of 1 mV) with which the GPES software is equipped.

Absorption spectra were recorded using the UV–VIS spectrophotometer SPECORD S100 from Carl Zeiss Technology with Win-Aspect software. The experimental conditions for absorption spectra were: integration time 25 ms and accumulation 1000 points.

Microvolumes were measured using EP-10 and EP-100 Plus Motorized Microliter Pipettes (Rainin Instruments, Woburn, USA). The pH measurements were carried out with a GLP 21 Crison pH meter.

All the graphs are treated and presented in Microcal Origin Version 6.0.

## 3. Results and discussion

The electrochemical behavior of quercetin [19], 8-oxoguanine [20], single and double stranded DNA at a GCE was briefly revisited in order to make it easier to identify the peaks occurring after quercetin–dsDNA interaction. The differential pulse voltammograms of quercetin are shown in Fig. 1A. The first oxidation peak 1 of quercetin, $E_p$ = +0.30 V, corresponds to the loss of two electrons and two protons from the 3′, 4′-dihydroxy substitute on the ring B, a reversible process giving *o*-quinone species which can undergo rearrangements strongly dependent of the other groups present in the molecule [21]. Also, some flavonoids were reported to form dimers at the electrode surface, thus peak 2, $E_p$ = +0.45 V, might be due to the formation of quercetin-dimers via a quinonoid structure [22,23]. Furthermore, peak 3, $E_p$ = +0.69 V, corresponds to the oxidation of the hydroxyl group at C3 in the ring C while the last peak 4, $E_p$ = +0.87 V, is due to the oxidation of 5,7-dihydroxy substitutes [21]. At the end of each experiment, the electrode was rinsed with water and transferred to acetate buffer. After transferring the electrode into the supporting electrolyte, the differential pulse voltammogram obtained showed only one anodic signal at $E_p$ = +0.32 V, corresponding to peak 1, showing that after quercetin adsorption at the electrode surface only the 3′, 4′-dihydroxy substitute on the ring B, the catechol moiety, is available for oxidation. Also, in Fig. 1A a differential pulse voltammogram of 8-oxoguanine showing that a considerable overlapping could occur between the 8-oxoguanine oxidation peak, $E_p$ = +0.45 V, and quercetin peak 2 is included. That means there is greater

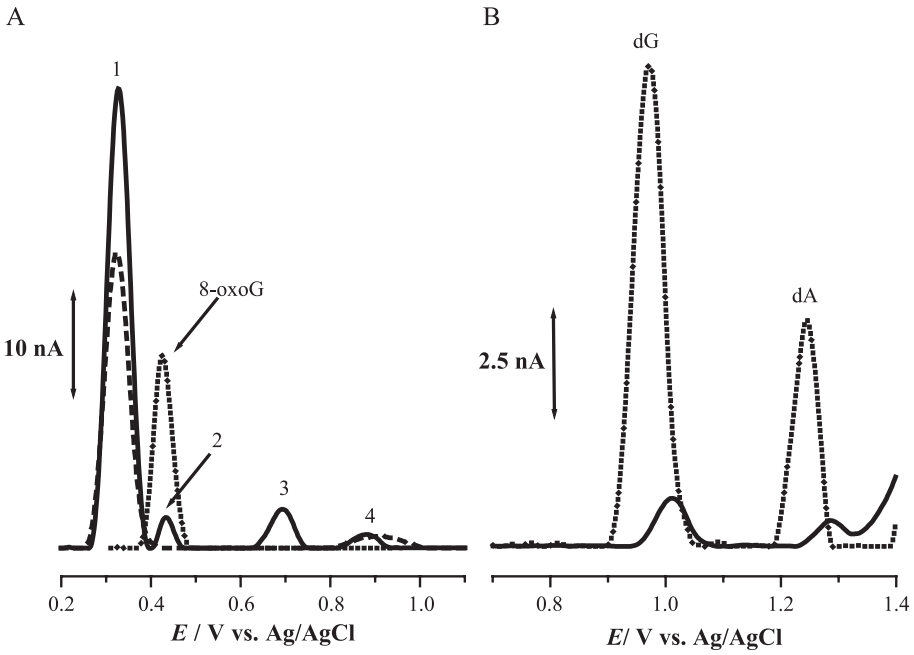


Fig. 1. Differential pulse voltammograms in pH 4.3, 0.1 M acetate buffer of: (A) 100 μM quercetin (▬), adsorbed quercetin (----) and 2 μM 8-oxoG (•••); (B) 50 μg $ml^{-1}$ (•••) ssDNA and dsDNA (▬). Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s.

difficulty in identification if these species exist together in the same solution.

The differential pulse voltammogram for the oxidation of dsDNA at GCE in pH 4.5, 0.1 M acetate buffer shows two tiny signals corresponding to the oxidation of guanosine [24], $E_p$=+1.02 V, and adenosine [25], $E_p$=+1.27 V, residues in the polynucleotide chain, while in the case of ssDNA the peaks are about 10-fold higher showing a small shift to lower potential values, thus meaning easier oxidation of guanosine and adenosine. In fact, the small peaks obtained in solutions of dsDNA using differential pulse voltammograms show the greater difficulty for electron transfer from inside the rigid double-stranded DNA to the electrode surface than from the more flexible single-stranded DNA where the bases can be in close proximity to the electrode surface.

### *3.1. Analysis of quercetin–DNA interaction in the incubation solutions*

The electrochemical study of quercetin–dsDNA interaction in solution was carried out by two different types of experiment: incubation of dsDNA with quercetin in the absence and in the presence of $CuSO_4$ followed by the detection at GCE directly in solution. Although saturated quercetin solutions have been used in this study greater quercetin solubility was observed in dsDNA-containing solutions, probably due to its interaction with the DNA double strand.

In the first series of experiments, 50 μg $ml^{-1}$ dsDNA were incubated with different concentrations of quercetin in the absence and in the presence of $CuSO_4$, prior to differential pulse voltammetry measurements. The GCE surface was cleaned between each measurement to avoid current decrease due to strong adsorption of both quercetin and DNA [22,26] after successive scans.

Differential pulse voltammogram of 50 μg $ml^{-1}$ dsDNA in the presence of 100 μM saturated quercetin in solution, Fig. 2A, shows quercetin oxidation peaks followed by the two anodic peaks corresponding to the oxidation of the purinic DNA bases. Small positive shifts of about 20 mV in the oxidation potential of quercetin are observed proving that an interaction between quercetin and DNA had occurred.

On the other hand, the differential pulse voltammograms obtained after 24 h of incubation of 50 μg $ml^{-1}$ dsDNA with 100 μM quercetin in the presence of 50 μM $CuSO_4$ in solution show different features, Fig. 2A. The first quercetin oxidation peak 1 completely disappeared followed by a very big increase of the peak at the potential of +0.45 V, which indicates the formation of at least one new product. At the same time, an increase in the guanosine and adenosine oxidation peaks was observed, showing that changes in dsDNA structure had occurred.

The tremendous increase of the peak at +0.45 V due to the DNA interaction with quercetin in the presence of Cu(II) ions was further investigated as a function of quercetin and $CuSO_4$ concentrations as well as of incubation time.

Samples containing 50 μg $ml^{-1}$ dsDNA and 100 μM quercetin were analyzed after 24 h of incubation with different concentrations (5 up to 50 μM) of $CuSO_4$. A progressive increase of the peak current takes place up to a concentration of 40 μM $CuSO_4$ and after a constant value

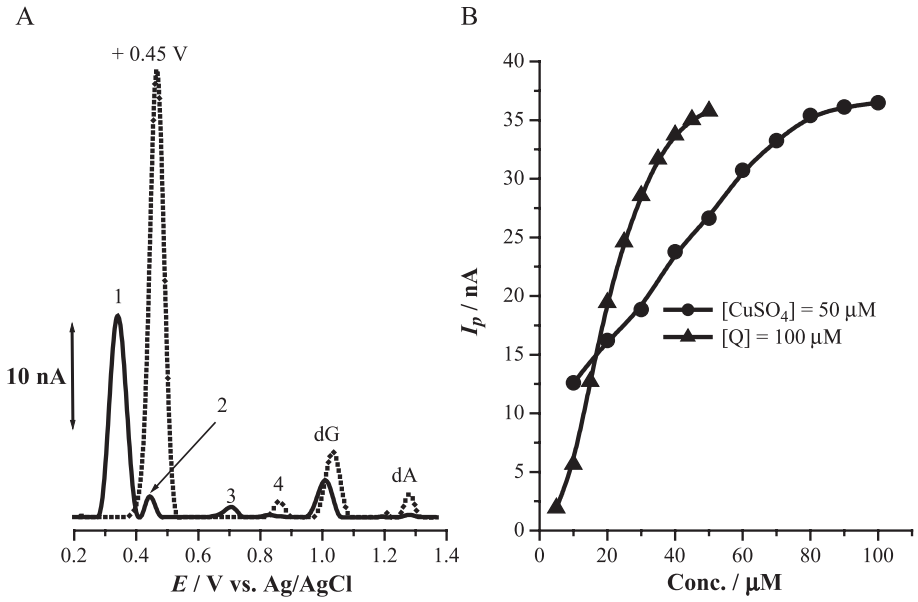


Fig. 2. (A) Differential pulse voltammograms in pH 4.3, 0.1 M acetate buffer of 50 μg $ml^{-1}$ dsDNA in presence of: 100 μM quercetin (▬) and 100 μM quercetin incubated for 24 h with 50 μM $CuSO_4$ (•••). Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s. (B) Influence of quercetin (●) and $CuSO_4$ (▲) concentrations on the oxidation peak current at +0.450 V.

of 37 nA was reached, Fig. 2B. Addition of more $CuSO_4$ to this sample shows no effect on the peak current at +0.45 V even if quercetin molecules in solution were still available to bind Cu(II) ions. This could be explained supposing that quercetin interacts with DNA at preferred sites [9]. When excess quercetin is present in the solution, all these sites are occupied, so that none remain in DNA to which quercetin–Cu(II) complex could bind and therefore the DNA could not be further damaged.

Samples of 50 μg $ml^{-1}$ dsDNA containing 50 μM $CuSO_4$ were also incubated with different concentrations of quercetin (10 up to 100 μM) and analyzed after 24 h. A similar behavior was observed showing a gradual increase of the peak amplitude with quercetin concentration up to 75 μM where it levels of and a value of 37 nA was reached, Fig. 2B. The addition of excess quercetin to the sample showed no effect on the formation of the new product because there are no more Cu(II) ions available to bind to quercetin molecules, thus to damage DNA.

From these results, it was observed that solutions containing 100 μM quercetin incubated with 50 μM $CuSO_4$ are the most effective for the formation of the quercetin–Cu(II) complex. Therefore, these concentrations were chosen for further characterization of the DNA–quercetin–Cu(II) interaction.

The effect of the incubation time on the appearance of the +0.45 V peak was studied in samples containing 50 μg $ml^{-1}$ dsDNA incubated with the quercetin–Cu(II) complex. The differential pulse voltammograms were recorded sequentially after different incubation periods. Between consecutive scans, the electrode surface was always cleaned to avoid blocking of the electrode with oxidation products from a previous anodic scan. Differential pulse voltammograms were recorded after the addition of Cu(II) ions and after 30 and 100 min of incubation with $CuSO_4$, Fig. 3A. The oxidation peak 1 of quercetin decreased gradually in time while the peak at +0.45 V increased with the incubation period. On the other hand, a slow increase in the amplitudes of guanosine and adenosine oxidation peaks is observed. In Fig. 3B, a plot of the measured currents of the peak at +0.45 V with the incubation time is presented. A constant increase of the peak amplitude takes place along the first 4 h of incubation then it levels at about 40 nA.

This results do not yet enable a conclusion concerning the type of damage produced by the quercetin–Cu(II) complex to DNA. Nevertheless, small changes in the current of guanosine and adenosine peaks could be observed indicating that modifications into the DNA structure had occurred.

In order to clarify the types of change taking place in dsDNA during its interaction with quercetin, the differences in the absorption spectra were monitored with time. Thus, samples containing 2.5 μg $ml^{-1}$ dsDNA were incubated with 25 μM quercetin for different periods of time in the absence and in the presence of 12 μM $CuSO_4$. Absorption spectra of 25 μM quercetin, curve (1) and 2.5 μg $ml^{-1}$ dsDNA, curve (2), are shown in Fig. 4. A typical main absorption band at 260 nm is observed in dsDNA while quercetin shows only small bands, the first at 230 nm followed by two other bands at 255 nm, and at 370 nm. The very small absorption of quercetin can be explained by its very low solubility in polar solvents. Absorption spectra of 25 μM quercetin in the presence of 12 μM $CuSO_4$ were also recorded but no difference was observed in these conditions.

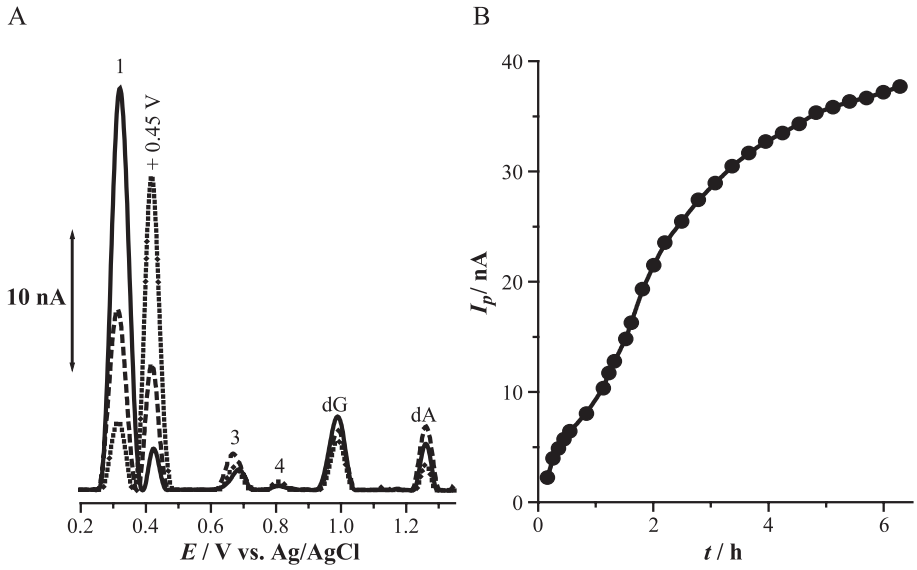


Fig. 3. (A) Differential pulse voltammograms in pH 4.3, 0.1 M acetate buffer of 50 μg $ml^{-1}$ dsDNA incubated with 100 μM quercetin and 50 μM $CuSO_4$ after: 0 min (▬), 30 min (----) and 100 min (•••) incubation time. Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s. (B) Influence of the incubation time on the oxidation peak current at +0.45 V.

When DNA and quercetin were mixed, after 10 h of incubation, the spectra exhibit the main absorption bands common to both dsDNA and quercetin, curve (3), and a hyperchromic effect was observed. A very small increase in the absorption maximum at 260 nm can be attributed to changes in the dsDNA due to the intercalation [17,18] of quercetin molecules. The interaction between quercetin and dsDNA could induce the observed greater solubility of quercetin, this explaining the hyperchromic effect at the maximum at 350 nm.

A sample solution containing dsDNA, quercetin and $CuSO_4$ after 10 h incubation, curve (4), showed an increase of about 30% in the dsDNA absorption band and the disappearance of the quercetin absorption band at 370 nm. The increase of the 260 nm maximum in dsDNA, from curve (2) to curve (4), is proof that degradation of DNA occurred after interaction with quercetin–Cu(II) complex. However, the hyperchromicity shown in the 260 nm band proves that the opening of the dsDNA helix occurred.

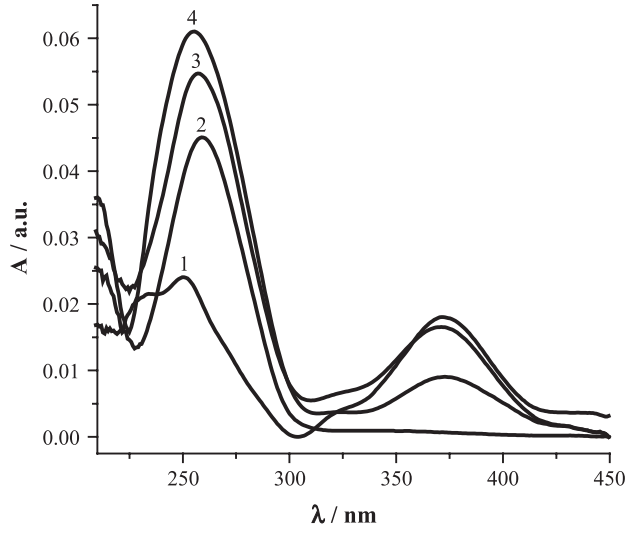


Fig. 4. Absorption spectra of: (1) 25 μM quercetin; (2) 2.5 μg $ml^{-1}$ dsDNA; (3) 2.5 μg $ml^{-1}$ dsDNA incubated for 10 h with 25 μM quercetin and (4) 2.5 μg $ml^{-1}$ dsDNA incubated for 10 h with a mixture of 25 μM quercetin and 12 μM $CuSO_4$.

Electrochemical experiments carried out in the solution did not give much information concerning the type of possible DNA damage. Nevertheless, the formation of a new electroactive product was detected and spectrophotometric measurements clearly showed that changes in the dsDNA structure had occurred. It was also observed that quercetin does not damage dsDNA in the absence of Cu(II) ions.

### 3.2. Control experiments

Control experiments have been carried out in order to clarify the electrochemical importance of Cu(II) ions in quercetin causing DNA damages.

The interaction between quercetin and $CuSO_4$ has been studied. The effect of incubation time on the quercetin oxidation peaks was studied in a solution containing 100 μM quercetin and 50 μM $CuSO_4$. The differential pulse voltammograms were recorded sequentially after different incubation periods and they are presented in Fig. 5A. Between each measurement, the electrode surface was always polished. The presence of all quercetin oxidation peaks is observed. Also, the voltammogram obtained immediately after the addition of $CuSO_4$ shows peaks several times much smaller than in the case of 100 μM quercetin. The peaks gradually decrease with increasing incubation period, as is clearly seen in the currents of peaks 1 and 2 in

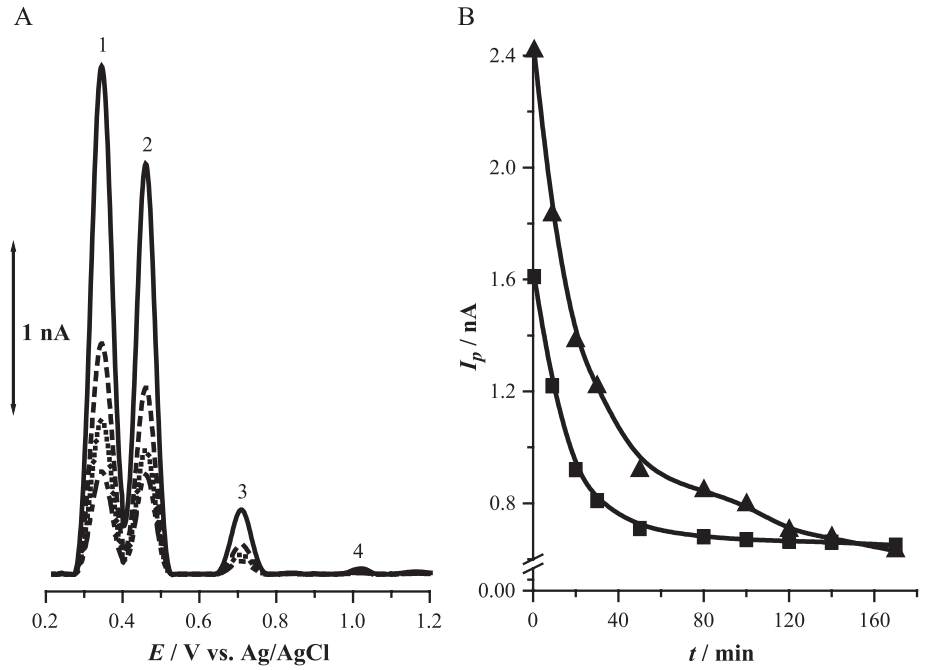


Fig. 5. (A) Differential pulse voltammograms obtained in 100 μM quercetin incubated for 0.5 (▬), 20 (----), 50 (•••) and 160 min with 50 μM $CuSO_4$ in pH 4.3, 0.1 M acetate buffer. Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s. (B) Quercetin oxidation currents peak 1 (▲) and peak 2 (■) with incubation time.

Fig. 5B. A fast decrease of the peaks takes place during the first 30 min of incubation and then it levels at about 0.6 nA Therefore, in all the experiments previously described, the interaction between dsDNA and quercetin–Cu(II) complex has been studied using mixtures of quercetin with $CuSO_4$ incubated for at least 2 h.

In Fig. 6A, a differential pulse voltammogram obtained in a solution of 100 μM quercetin incubated during 2 h with 50 μM $CuSO_4$, with the electrode immersed for 10 min in the solution before recording the voltammogram, is shown. The occurrence of all four quercetin oxidation peaks can easily be observed. The electrode was polished and im-

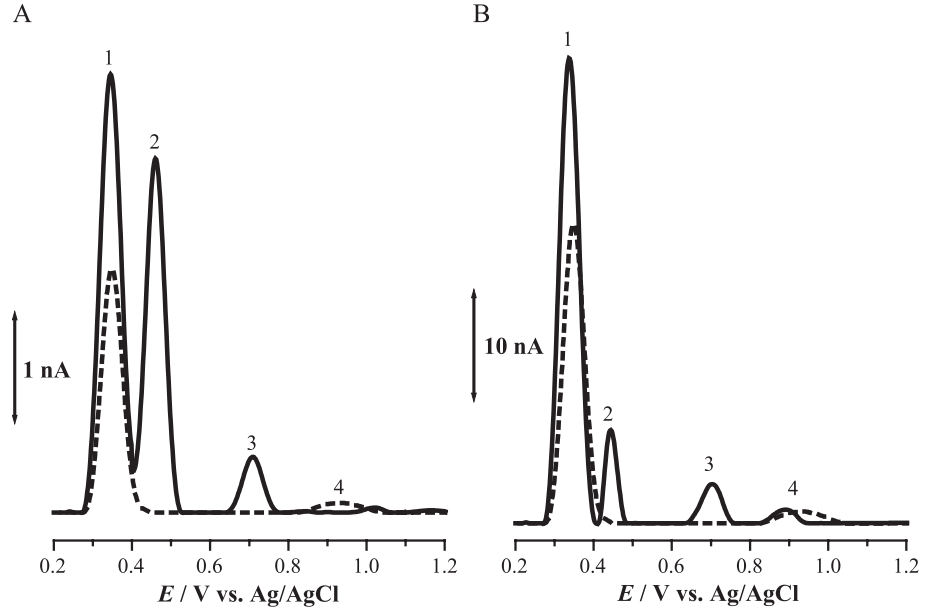


Fig. 6. Differential pulse voltammograms in pH 4.3, 0.1 M acetate buffer with GCE after 10 min of adsorption in: (A) quercetin–Cu(II) complex prepared from a solution of 100 μM quercetin incubated with 50 μM $CuSO_4$ obtained in: the incubated solution (▬) and after transferring the electrode to acetate buffer (----); (B) 100 μM quercetin solution (▬) and after transferring to acetate buffer (----). Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s.

mersed for 10 min in the previous solution of 100 μM quercetin incubated during 2 h with 50 μM $CuSO_4$. After adsorption, it was washed with water and transferred to acetate buffer where another differential pulse voltammogram was performed. After this procedure, one main peak at +0.35V corresponding to the quercetin oxidation peak 1 and a smaller signal at +0.87 V which corresponds to peak 4 were observed. This shows that the quercetin–Cu(II) complex formed in the solution does not adsorb at the electrode surface.

In another experiment, a clean electrode was kept for 10 min in a solution containing only 100 μM quercetin and a differential pulse voltammogram was recorded showing all four quercetin oxidation peaks, Fig. 6B. The electrode was cleaned and after 10 min adsorption in the previous quercetin solution the electrode was washed with deionized water and transferred to acetate buffer. A differential pulse voltammogram recorded with quercetin adsorbed at the GCE surface is shown in Fig. 6B. The main feature in this voltammogram is the occurrence of quercetin oxidation peaks 1 and 4. No other additional signals, namely at a potential of +0.45 V, were observed.

The interaction between ssDNA or guanine free polyhomonucleotides, specifically poly[A] and quercetin or quercetin–Cu(II) complex was investigated.

Differential pulse voltammogram of 50 μg $ml^{-1}$ ssDNA in the presence of 100 μM saturated quercetin in the solution, Fig. 7A, showed quercetin oxidation peaks followed by two large anodic peaks corresponding to the oxidation of DNA purinic bases, guanine and adenine. On the other hand, the differential pulse voltammogram obtained after 2 h of incubation of 50 μg $ml^{-1}$ ssDNA with 100 μM quercetin in the presence of 50 μM $CuSO_4$ in the solution showed different features, Fig. 7A. As in the case of dsDNA, the decrease of the first quercetin oxidation peak, peak 1, is followed by a very big increase of the peak at the potential of +0.45 V, which indicates the formation of a new product. At the same time, a small increase in the guanosine and adenosine oxidation peaks was observed. The breakage of the intra-strand hydrogen bonds formed between ssDNA complementary bases might be responsible for the small increase of guanosine and adenosine peaks observed after interaction of ssDNA with the quercetin–Cu(II) complex.

In order to obtain more information about the origin of the big peak at +0.450 V observed after quercetin–Cu(II) interaction with either ssDNA or dsDNA, control experiments of the interaction of quercetin or quercetin–Cu(II) with guanine free poly[A] were performed. A differential pulse voltammogram of 50 μg $ml^{-1}$ poly[A] in the presence of 100 μM saturated quercetin in the solution, Fig. 7B, showed quercetin oxidation peaks followed by a large anodic peak corresponding to the oxidation of adenosine residues at $E_p$=+1.27 V. Additionally, differential pulse voltammograms were recorded in the solution after addition of 50 μM $CuSO_4$. No oxidation peak at +0.450 V was obtained although a remarkable decrease of the height of quercetin oxidation peak 1 was observed after 10 h of incubation. At the same time, the adenosine oxidation peak maintained the same current, independent of the incubation period. This experiment clearly shows that the increase of the peak at +0.450 V is related with the presence of guanine residues in the DNA strand.

The behavior of dsDNA in the presence of Cu(II) ions was also studied in the solution. Solutions containing 50 μg $ml^{-1}$ dsDNA have been incubated for 24 h with 50 μM

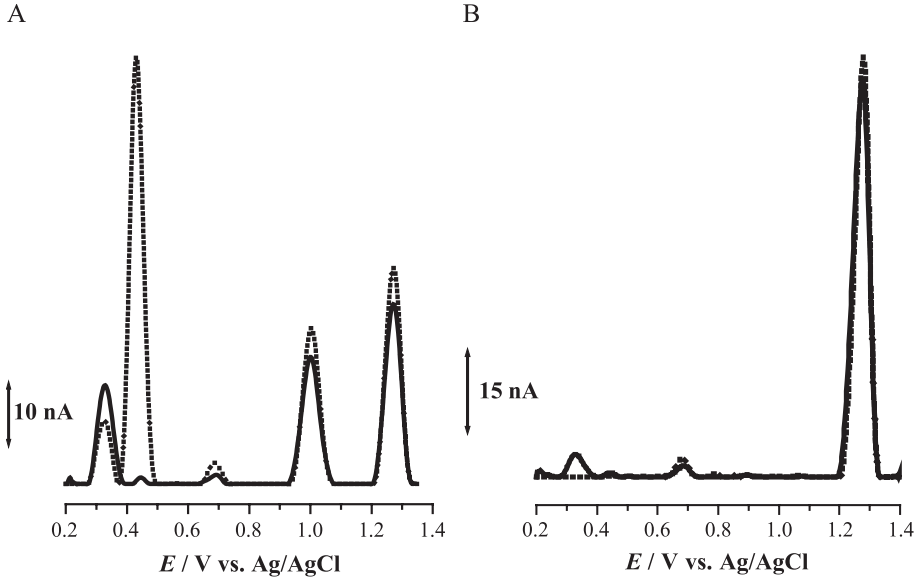


Fig. 7. Differential pulse voltammograms obtained with the GCE in pH 4.3, 0.1 M acetate buffer, after incubation for 10 h with 100 μM quercetin before (—) and after (•••) addition of 50 μM $CuSO_4$ to: (A) 50 μg $ml^{-1}$ ssDNA and (B) 50 μg $ml^{-1}$ poly[A]. Scan rate 5 mV $s^{-1}$, pulse amplitude 50 mV, pulse width 0.07 s.

$CuSO_4$ and then analyzed using differential pulse voltammetry. No differences in the dsDNA oxidation behavior were observed during these experiments.

### *3.3. Interaction mechanism between DNA and quercetin–Cu(II) complex*

A weak interaction between DNA and quercetin was found to take place in the incubated solutions. On the other hand, the present results give evidence that the binding reaction between quercetin and Cu(II) complex ions occurs and leads to the formation of a complex which does not adsorb at the GCE surface but strongly interacts with DNA. Also, as seen in the control experiments the incubation of dsDNA with Cu(II) ions does not have any effect on the voltammetric features of dsDNA. Therefore, the tremendous increase of the peak at +0.45 V is clearly due to the quercetin–Cu(II) complex intercalation into the DNA helix.

The damage produced to DNA by quercetin–Cu(II) complexes was recognized using differential pulse voltammetry and spectrophotometry, and could be explained considering the effect of the generation of highly reactive oxygen species [27] formed during the reaction of quercetin and Cu(II) ions [9]. The differential pulse voltammetric experiments to investigate the interaction of DNA with the quercetin–Cu(II) complex showed the appearance of a peak at a potential of +0.450 V which proves the formation of a new product. Different processes could occur and then the peak at +0.45 V observed after DNA interaction with quercetin–Cu(II) complex could be due to oxidation of different species present in the incubated solutions. Quercetin alone gives rise to a peak at +0.450 V which decreases with the incubation time in solutions containing quercetin and Cu(II) ions. However, in this work it was proved that the peak at +0.450 V does not appear any more when guanine free poly[A] is incubated with quercetin–Cu(II) complex. Therefore, the peak at +0.45 V in solutions containing DNA and quercetin–Cu(II) complex is due to the oxidation of 8-oxoguanine [20].

## 4. Conclusions

This work has shown experimental evidence of the interaction of quercetin with dsDNA and may contribute to the understanding of the mechanism of action of this flavonoid. Whereas a very weak interaction between quercetin and DNA was found to take place in the solution, the addition of Cu(II) ions to the DNA–quercetin solution has shown that a deep degradation of DNA helix takes place. Using electrochemical and spectrophotometric techniques, it was observed that the dsDNA damage occurred with time which suggests that the quercetin–Cu(II) complex intercalates with dsDNA and slowly interacts with it causing breakages of the hydrogen bonds. The formation of new products such as 8-oxoguanine, due to the DNA interaction with quercetin–Cu(II) complex was explained.

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