

# **Semi-circular Sweep Voltammetry.**

## **Bio-analytical Applications**

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## **Abstract**

A novel voltammetric method applying a semi-circular potential sweep is applied to the simultaneous electroanalytical determination of solutions containing two components with similar oxidation potentials which precludes their resolution using conventional voltammetric methods including linear sweep, square wave and pulse voltammetries. Three such biologically important mixtures, ascorbic acid / acetaminophen, glucose / ethanol and hydroquinone / catechol were studied, analytical methods developed and the method of semi-circular sweep voltammetry shown to give notable advantages over the other conventional analytical voltammetries in terms of signal resolution and the sensitivity of the detection. Favourable accuracy was obtained using electrodes with either simple or no modification in the established linear detection ranges.

## **Keywords**

Semi-circular Sweep Voltammetry; Ascorbic Acid; Hydroquinone; Glucose; Selective Voltammetric Detection

## 1. Introduction

Analytical voltammetry is usually performed using a linear potential sweep and measuring the resulting currents. Often pulses or oscillations are imposed on the sweep in the form of square wave or differential pulse voltammetry with a significant increase in sensitivity and, with careful analysis, increased information about the electrode process of interest (Brett and Brett 1993; Molina and González 2016; Wang 2006). Such approaches to analysis offer speed of measurement, require low cost equipment and often generate attractively low limits of detection coupled with good sensitivity. As a result amperometric chemical sensors dominate the market for blood glucose sensors (Toghill and Compton 2010; Wilson and Turner 1992) and are strong competitors in the gas sensing area (Xiong and Compton 2014) building on the original Clark cell for oxygen detection with many companies now offering electrochemical sensors for carbon monoxide (smoke detectors), ammonia, hydrogen sulphide, carbon dioxide and nitrogen oxides (Honeywell 2020; Alphasense 2020; Citytech 2020; Sensirion 2020). That said one generic weakness of amperometric detection concerns the selectivity of measurement which is overcome, for example, in the case of glucose detection by employing enzymes to impose the selectivity and making the measurement indirectly, often via the detection of hydrogen peroxide. However this weakness, in the opinion of the authors, may account for the rather niche status of amperometric electrochemical bio-sensors within the entire field of bio-analytical measurements viewed holistically.

We have recently introduced an innovative approach to voltammetry which is not based on a linear potential sweep but rather on an increasing potential where the instantaneous potential scan rate varies with potential (Uchida et al. 2019a; Uchida et al. 2018a, b, 2019b; Uchida et al. 2017, 2018c). Most notably, but not exclusively (Uchida et al. 2017, 2018c), this work has utilised a semi-circular potential sweep in which the instantaneous scan rate varies from zero to near infinite (within the limitations of the controlling electronics) at the mid-point

of the scan, as shown in Figure 1. This has been used for fundamental studies of some redox couples. Recently we have considered the possible application of such variable scan rate potential sweep methods in electro-analysis. In particular it is interesting to explore whether semi-circular voltammetry (SCV) can be usefully applied to enhance the selectivity of electroanalytical detection noting that the magnitude of the current response in linear sweep voltammetry increases markedly with scan rate both for diffusional and thin-layer/adsorptive systems (Compton and Banks 2018). As a consequence one peak in a voltammogram might be enhanced in comparison with another peak if the former experiences a greater instantaneous voltage scan rate than the latter. Proof of concept of this idea was presented in the successful voltammetric resolution of chlorophyll a and b in their mixtures despite them having closely similar oxidation potentials (Wang et al. 2020).

In this paper we apply the SCV technique to 3 different bio-analytical challenges in each of which a mixture of two components with near identical redox potentials is interrogated to explore and validate the generality of the approach especially in the context of biosensors. These mixtures are the detections of ascorbic acid (AA)/ acetaminophen (AC), hydroquinone (HQ) /catechol (CC) and glucose (Glu)/ethanol mixtures. AC is a widely used analgesic and

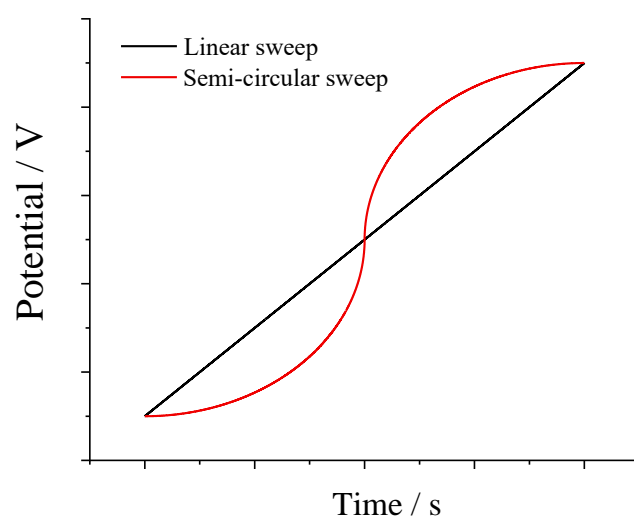


Figure 1. Waveforms of cyclic voltammetry (black line) and semi-circular sweep voltammetry (red line) at the same average scan rate.

antipyretic drug which co-exists with AA, an essential water-soluble vitamin in various biological matrices (Bosch et al. 2006; Săndulescu et al. 2000). The mixtures of AA and AC were also seen in some pharmaceutical formulations as the presence of AA was shown to intensify the therapeutic effect of AC whilst compensating for its hepatotoxicity (Padayatty et al. 2003). HQ and CC are two isomers of dihydroxybenzene that coexist as pollutants in environmental samples due to their high toxicity and low degradability (Xie et al. 2006). Ethanol is one of the major interferences for blood glucose detection (Toghill and Compton 2010). The concentrations of ethanol and glucose are also used as quality indicators for alcoholic beverages during fermentation (Kitagawa et al. 1991; Shkotova et al. 2016). The selective determinations of the individual analytes in the above mixtures are of great importance in the corresponding areas of medical monitoring in biological fluids, food and pharmaceutical quality control and environmental pollution assessment. Through the investigations of these systems, the applicability of SCV technique and its advantages over conventional voltammetric techniques are demonstrated.

## **2. Results and Discussion**

In the following sections and in the SI, three different model analytical systems each consisting of two components are examined voltammetrically so as to identify the merits of semi-circular voltammetry (SCV). In each case under conventional cyclic voltammetry (CV), the voltammetric signals from the two components overlap to a significant extent so as to make the analytical determination of the mixture difficult or impossible using linear sweep voltammetry at a planar electrode. Specifically mixtures of ascorbic acid (AA) / acetaminophen (AC), hydroquinone (HQ) / catechol (CC) and glucose (Glu) / ethanol are used as model systems to explore the value and possible superiority of SCV in the simultaneous determination of individual species in each mixture. In each example system, first, the electrochemistry of

the studied species on the working electrode of interest was examined using CV. Next, the performance of SCV was compared with the other commonly used voltammetric methods, including linear sweep voltammetry (LSV), square wave voltammetry (SWV) and differential pulse voltammetry (DPV). Meanwhile, in combination with the use of SCV, the development of specific electrochemical detection and quantification methods were demonstrated for each system. In section 2.1, a method of quantifying the AC contents of real pharmaceutical samples is developed. In section 2.2, a GC electrode is modified with MWCNTs by a dropcasting method to better resolve the isomers of HQ and CC and the effects of SCV on the sensitivity are explored. In section S6, the use of a Ni electrode to develop non-enzymatic sensors for systems containing both glucose and ethanol is advocated.

## 2.1 Ascorbic Acid and Acetaminophen

### 2.1.1 Electrochemical Behaviour of Ascorbic Acid and Acetaminophen

The separate electrochemical behaviour of ascorbic acid (AA) and acetaminophen (AC) at a GC electrode were first investigated using CV. The individual cyclic voltammetric responses of 1mM AA (red line) and AC (blue line) in pH 7.4 PBS were recorded at  $50 \text{ mVs}^{-1}$  as shown in Figure 2 (A). The oxidation peak occurred at 0.32 V vs SCE for AA and 0.44 V vs SCE for AC. The effects of variable scan rates on the peak currents of AA and AC were studied (Figure 2(B) and 3(C)). The peak currents of both AA and AC exhibited linear dependences on the square roots of scan rates in the range of  $25\text{-}500 \text{ mVs}^{-1}$  (Inset of Figure 2(B) and 2(C)), suggesting the electro-oxidation of AA and AC are both diffusion-controlled processes. The electro-oxidations of AA and AC at the studied pH have been reported in the literature both as two electron, two proton processes (Inset of Figure 2(A)) (Hu and Kuwana 1986; Nematollahi et al. 2009; Rice et al. 1989). The transfer coefficient ( $\beta$ ) values for the two-electron transferred oxidation process of AA and AC were determined from the Tafel slopes in the corresponding Tafel analysis (Figure S1 and S2) to be 0.44 for AA and 0.78 for AC,

confirming that the oxidations of both AA and AC correspond to processes where the first-electron transfer is the rate determining step (Compton and Banks 2018). The diffusion coefficient of AA and AC at 298 K were calculated as  $5.9 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$  for AA and  $7.0 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$  for AC, using the irreversible multiple electron-transfer *Randles-Sevcik* equations (Compton and Banks 2018), assuming overall two-electron oxidations and the measured transfer coefficients. The values are in good agreement with literature values (Ensafi et al. 2010; Pandey et al. 2018; Ribeiro et al. 2012; Robinson et al. 1990).

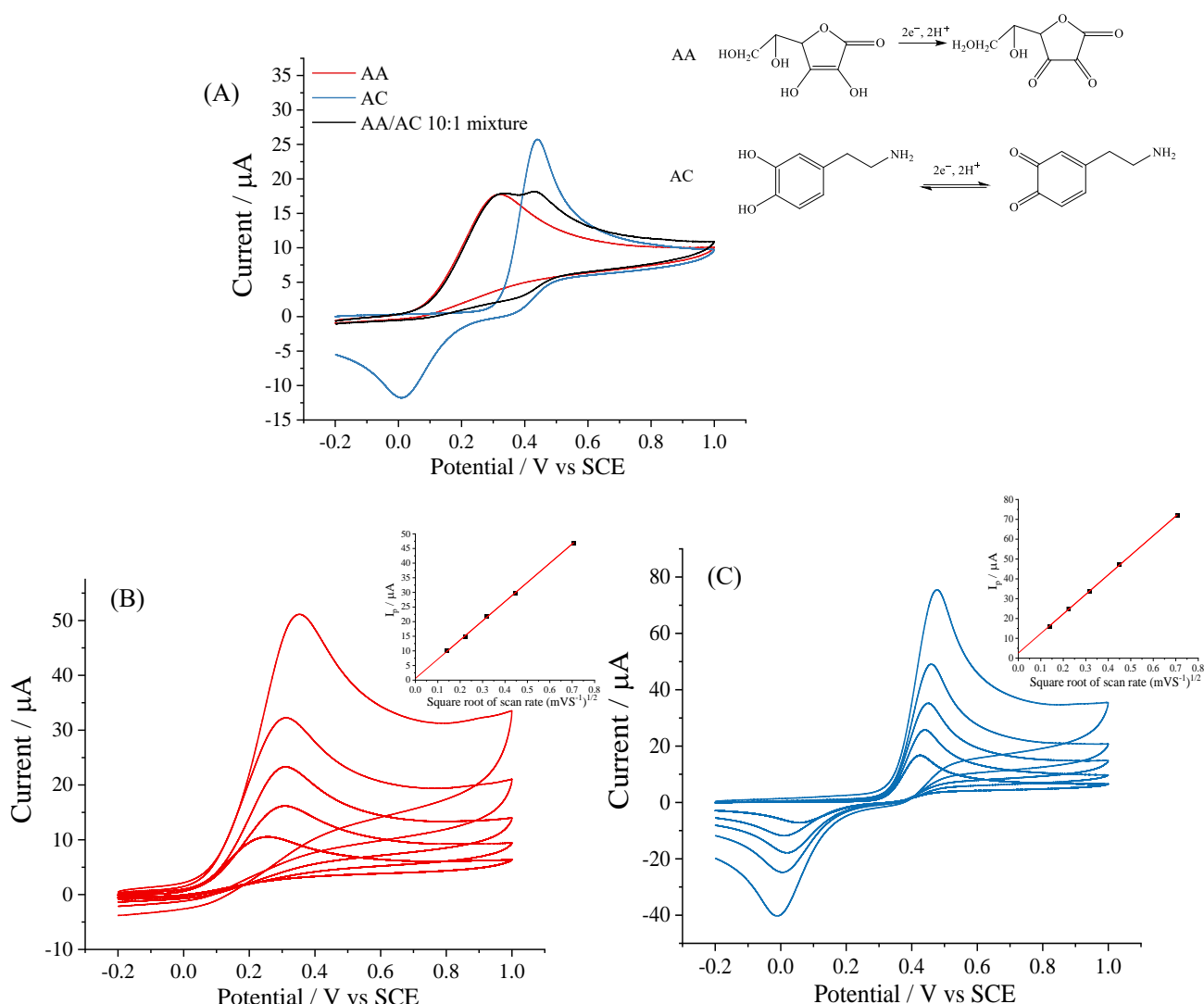


Figure 2. Triangular sweep cyclic voltammetric responses of (A) 1 mM AA, 1 mM AC and of a mixture containing 1mM AA and 0.1 mM AC at a scan rate of 50 mVs<sup>-1</sup>(B) 1 mM AA and (C) 1 mM AC at varying scan rates of 25 mVs<sup>-1</sup>, 50 mVs<sup>-1</sup>, 100 mVs<sup>-1</sup>, 200 mVs<sup>-1</sup>, 500 mVs<sup>-1</sup>, at GC electrode in PBS. Inset of A: The two-electron, two-proton oxidation of AA (upper) and AC (lower) (Hu and Kuwana 1986; Nematollahi et al. 2009; Rice et al. 1989). Insets of (B) and (C): plots of peak currents versus square roots of scan rates of (B) 1 mM AA and (C) 1 mM AC.

A cyclic voltammogram of the mixture containing 1 mM AA and 0.1 mM AC is shown in Figure 2 (A) (black line). Two broad, merged, strongly overlapping peaks can be seen near 0.33 V and 0.44 V vs SCE, belonging to AA and AC, respectively. The high level of overlap indicates that a more sensitive and selective voltammetric method offering better resolution was required for the analysis of such mixtures.

#### 2.1.2 Determination of Acetaminophen in the presence of Ascorbic Acid

Next, the electroanalytical responses of AC in the presence of high levels of AA were explored on a GC electrode. In order to evaluate the applicability of different voltammetric techniques for the detection of AC in AA/AC mixture system such that the optimal resolution of the voltammograms and sensitivity of detection can be obtained, the commonly used LSV, SWV, DPV techniques and the recently developed SCV method were employed and compared. As discussed above and previously (Uchida et al. 2018b, 2019b; Wang et al. 2020; Wang and Compton 2020), SCV applies a semi-circular wave over a chosen potential window, which generates a near infinite scan rate at the mid-point of potential windows (defined as  $E_{mid}$ ) and relatively low scan rates elsewhere. Thus it can selectively determine individual species in the mixtures by amplifying the signal closer to  $E_{mid}$  and relatively suppressing the signal further from  $E_{mid}$ . Voltammograms of 100  $\mu$ M AC in the presence of 1 mM AA and with varying potential windows were recorded as shown in Figure 3 (A), suggesting an optimised  $E_{mid}$  as 0.6 V vs SCE for the detection of AC where a scan amplitude of 0.7 V is used to further optimise the resolution of the voltammogram (Figure 3 (B)). A similar procedure was performed and the potential window for the voltammograms of 100  $\mu$ M AC in the presence of an even higher concentration of 5 mM AA was centred at 0.7 V vs SCE with a scan amplitude of 0.7 V applied. Figure 3 (C) and 3 (D) compare semi-circular voltammetric responses under the optimised potential windows with the linear, square wave and differential pulse



voltammetric responses of 100  $\mu\text{M}$  AC in the presence of 1 mM and 5 mM AA, at the same average scan rate of 50  $\text{mVs}^{-1}$ . It can be seen that LSV resulted in the poorest resolutions, whereas SWV, DPV and SCV were shown to separate the peaks of AA and AC to different extents. The peak separations in square wave, differential pulse, semi-circular voltammograms were 147 mV, 146 mV and 137 mV, all representing an analytically useful improvement over the value of 99 mV in the linear sweep voltammogram. In particular, SCV provides the refined and best-resolved peaks at 0.32 V, 0.45 V vs SCE in the 1 mM AA system and 0.29 V, 0.55 V vs SCE in the 5 mM AA system since the current responses generated at the potential of AC were closer to  $E_{\text{mid}}$  and largely amplified relative to the competing signal. The additional peak near  $E_{\text{mid}}$  arises from the nominally infinite transient scan rate (within the limitations of the potentiostat electronics) leading to strong capacitive currents (Uchida et al. 2018b; Wang et al. 2020). SCV is thus shown to be advantageous in the way that it can selectively amplify the current responses of species present in low concentrations despite the presence of another species of similar oxidation potential with 10- or 50-fold of the concentrations.

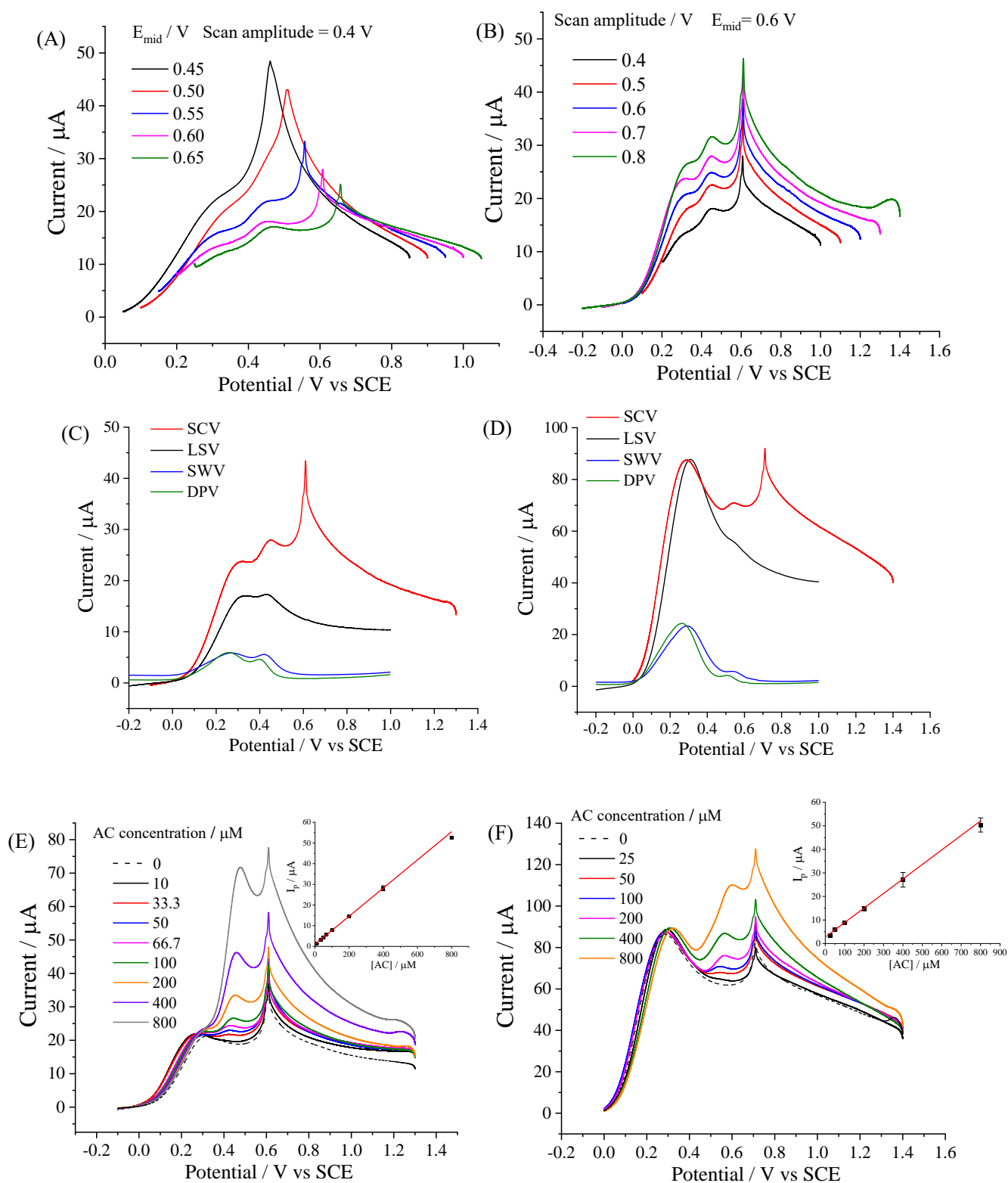


Figure 3. Semi-circular sweep voltammetric responses of 100  $\mu\text{M}$  AC in the presence of 1 mM AA at the GC electrode recorded at potential windows with (A) varying  $E_{\text{mid}}$  (B) varying scan amplitudes. Semi-circular sweep, linear sweep, square wave and differential pulse voltammetric responses of 100  $\mu\text{M}$  AC in the presence of (C) 1 mM and (D) 5 mM AA. Semi-circular voltammetric responses of (E) 10-800  $\mu\text{M}$  AC in the presence of 1 mM AA and (F) 25-800  $\mu\text{M}$  AC in the presence of 5 mM AA. The  $E_{\text{mid}}$  of the potential windows used in SCV at the potential was 0.6 V vs. SCE in (C) and (E) and 0.7 V vs. SCE in (D) and (F). The scan amplitude and the average of scan rate used in (C)-(E) were 0.7 V and 50  $\text{mVs}^{-1}$ , respectively. Insets of (E) and (F): Plots of subtracted peak currents obtained from semi-circular voltammograms versus AC concentration.

Having compared the resolutions of the voltammograms, we next explored the sensitivity of detection under different types of analytical voltammetry. Additions of 10-800  $\mu\text{M}$  AC to 1 mM and 5 mM AA were conducted. The mixtures were prepared as three repeated sets and determined using SCV, LSV, SWV, DPV. Table S1 lists the linear detection ranges of AC and the peak current ( $I_p$ ) – concentration ( $[\text{AC}]$ ) relationships obtained from the semi-circular voltammograms in Figure 3 (E) and 3 (F) and the other voltammograms in Figure S3-S5. Similar linear ranges of 10-800  $\mu\text{M}$  and 25-800  $\mu\text{M}$  were found for the detection of AC in the 1 mM and 5 mM AA systems using the four studied voltammetric techniques. However, SCV showed the highest sensitivity of detection, showing a significant improvement of 2-3 times in comparison to the other techniques while retaining favourable linearity, even in the 5 mM AA system. It is concluded that SCV facilitates high-sensitivity detection of species in the presence of high interferent levels due to the amplified current responses and enhanced resolutions of the voltammograms.

### 2.1.3 Real sample analysis

As discussed in Section 2.1.2, SCV shows a significant advantage in determining the AC content in the mixtures of AA and AC over other techniques displaying high sensitivity and favourable resolution. To assess the reliability and feasibility of SCV for the electroanalysis of real samples, analysis of three separate real samples was performed. These were (A) commercial paracetamol capsules from the Sainsbury's, (B) the product Beechams Flu Plus from the Beechams and (C) the product EfferalganVitamineC from the UPSA. AC is the major component of the three studied medicinal samples and AA is present at a high level in the latter two cases. Three independent analyses were performed for each sample as described in section S1.3 and measured using SCV. As is apparent in Figure 4, the oxidation peak of AC was identified in the semi-circular voltammograms for all three medicines at 0.44

V vs SCE. A minor peak at ca. 0.2 V can be seen in Figure 4 (C), which is likely due to the contribution from a small amount of AA present in Effergal-VitamineC. The content of AC in the studied sample was determined using the calibration curve shown in Figure 3 (E), exhibiting results within a 6% deviation from the amount declared by the manufacturer (Table S1). Subsequently, known concentrations of standard solutions were added to ‘spike’ to each sample. Figure 4 depicts the resulting semi-circular voltammograms of samples with 50-200  $\mu\text{M}$  AC standard solutions added. The recovery was calculated as 93-110% for the three medicines (Table S3). Note that the recovery is close to 100%, indicating that AC is the only substance contributing to the measured current at the corresponding potential without interference caused by other compounds present in the studied real samples.

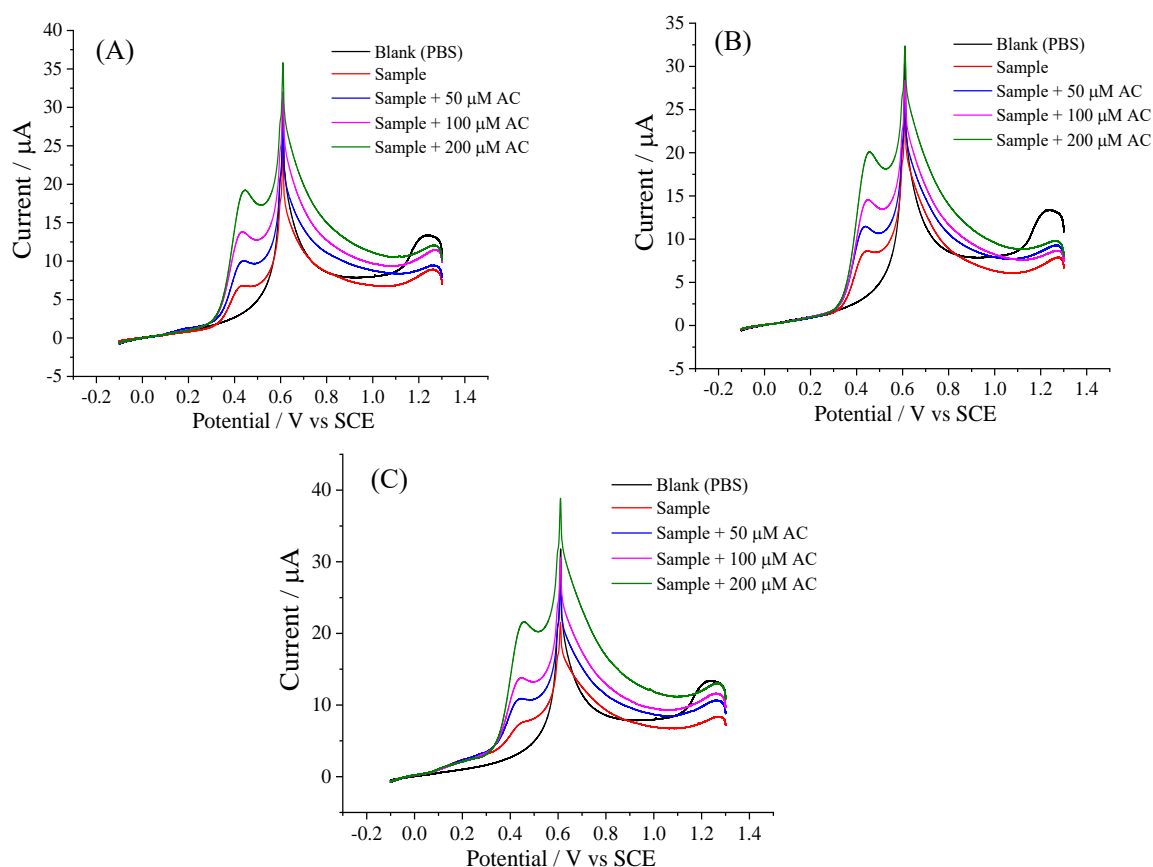


Figure 4. Standard additions of 50-200  $\mu\text{M}$  of AC solutions to the real samples of (A) Paracetamol (B) Beechams (C) Effergal at the potential window with  $E_{\text{mid}}=0.6$  V and the scan amplitudes was 0.7 V and the average scan rate was 50  $\text{mVs}^{-1}$ .

## 2.2 Hydroquinone and Catechol

### 2.2.1 Electrochemical Behaviour of Hydroquinone and Catechol

The cyclic voltammetric response of a 1:1 mixture of 0.5 mM hydroquinone (HQ) and catechol (CC) was first explored in pH 7.4 PBS buffer at an unmodified GC electrode, a carbon-nanotube modified screen printed electrode (CNT-SPE) and a MWCNT modified GC (MWCNT/GC) electrode. In the light of recently-developed voltammetric sensors for the dihydroxybenzene isomers using carbon-nanotube modified carbon-based electrodes (Ahammad et al. 2018; Hu et al. 2012; Wang et al. 2007; Yue et al. 2013; Zhao et al. 2009) MWCNTs/GCs were prepared using a simple dropcast method fully described in section S1.2. The dropcast volume of MWCNTs-acetone suspension was chosen as 20  $\mu$ L, which was the minimum volume to form a sufficiently thick layer (mass of 20  $\mu$ g, thickness estimated to be ca. 2.5  $\mu$ m - see Section 5 in SI) covering the GC surface such that a stable and reproducible voltammetric response was observed (Figure S10). As depicted by the dotted line in Figure 5 (A), at the unmodified GC electrode, the oxidation peaks of HQ and CC are merged into one broad peak at 0.30 vs SCE. The resolution of the voltammetric responses slightly improved in the case of the commercially supplied CNT-SPE, depicted by the dashed line in Figure 5 (A), where two strongly-overlapping peaks can be observed at 0.096 V and 0.20 V vs SCE. The solid line depicts the signals recorded at a MWCNTs/GC. Two well-defined, distinguishable, sharp peaks were observed at 0.074 and 0.19 V vs SCE. The MWCNT material, particularly when used as coating on GC electrode is thus shown to be analytically useful in resolving the present mixture as expected from literature reports. Accordingly we employed MWCNTs/GC for further simultaneous determinations of HQ and CC and to explore the further improvements offered by SCV.

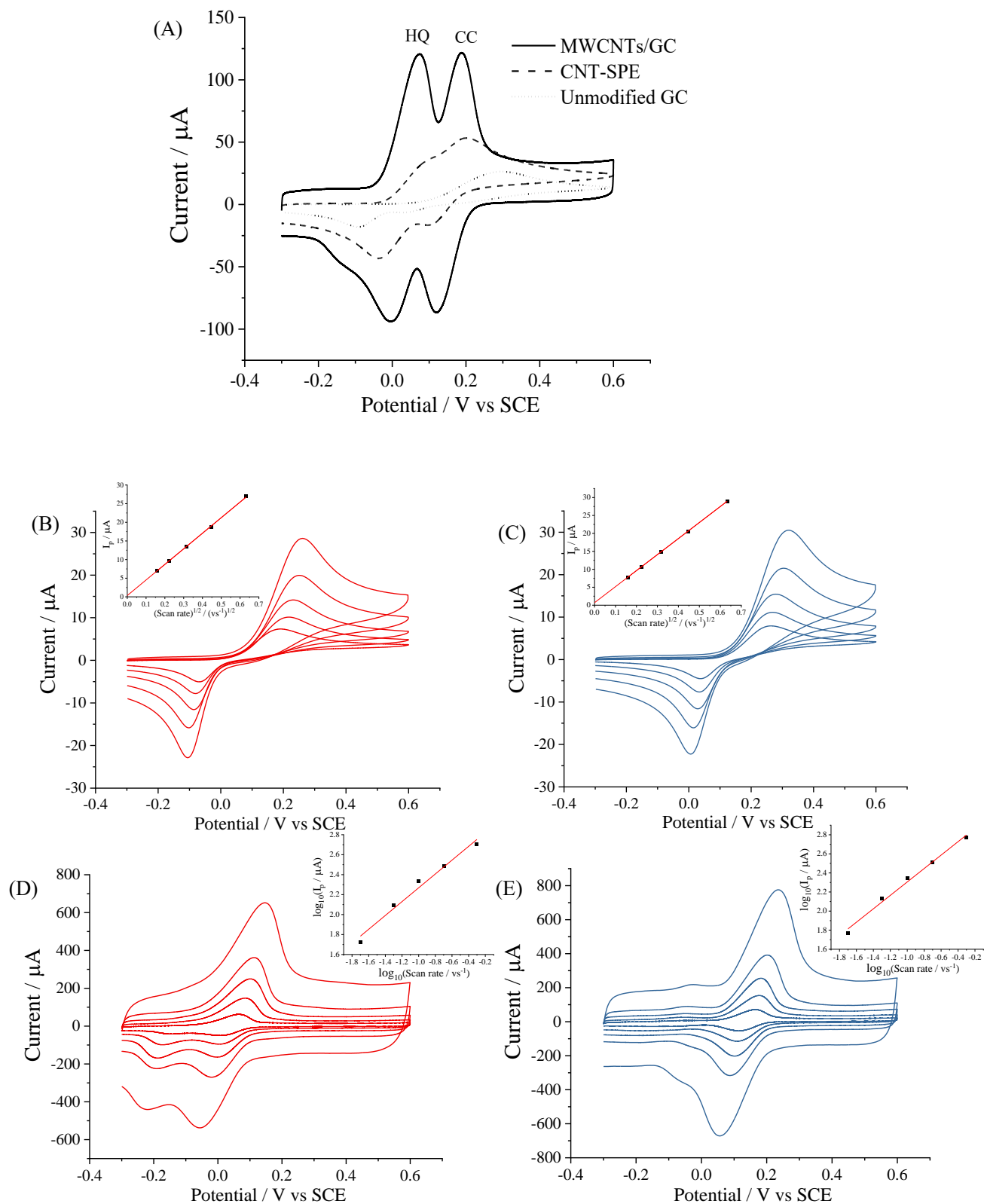


Figure 5. Triangular sweep cyclic voltammetric responses of (A) the mixture contain 0.5 mM HQ and 0.5 mM CC at unmodified GC electrode (dotted line), CNT-SPE (dashed line) and MWCNTs/GC electrode (solid line) at a scan rate of  $50 \text{ mVs}^{-1}$ , 0.5 mM HQ at (B) GC electrode and (D) and MWCNTs/GC electrode, 0.5 mM CC at (C) GC electrode and (E) MWCNTs/GC electrode, recorded at varying scan rates of  $20 \text{ mVs}^{-1}$ ,  $50 \text{ mVs}^{-1}$ ,  $100 \text{ mVs}^{-1}$ ,  $200 \text{ mVs}^{-1}$ ,  $500 \text{ mVs}^{-1}$ ; Insets of (B) and (C): plots of peak current versus square roots of scan rates; insets of (D) and (E): the log-log plots of peak current versus scan rate. The dropcast volume at GC electrode was  $20 \mu\text{l}$ .

Next, the effect of scan rate on the peak currents of the separate individual species HQ and CC was studied. The cyclic responses of 0.5 mM HQ or CC at the unmodified GC and the MWCNTs/GC electrode were recorded separately at the scan rates of 20-500 mVs<sup>-1</sup>, as shown in Figure 5 (B)-(E). Figure 5 (B) and 5 (C) depict the cyclic voltammograms and the plots of peak currents versus square root of scan rate obtained at unmodified GC electrode. Linear relations were found between the oxidation peak currents and the square root of scan rates, (Figure 5 (B) and 5 (C) Insets), suggesting the oxidation processes of HQ and CC were under diffusion-controlled at the unmodified GC electrode. The diffusion coefficients of HQ and CC were estimated using the peak currents measured at unmodified GC electrode via irreversible multiple electron-transfer *Randles-Sevcik* equation. Assuming the overall two electron transfer (Enache and Oliveira-Brett 2011) and the transfer coefficient was 0.5, the diffusion coefficients were found to be  $7.9 \times 10^{-6}$  cm<sup>2</sup>/s for HQ and  $9.0 \times 10^{-6}$  cm<sup>2</sup>/s for CC, consistent with the values reported in literature (Burestedt et al. 1996; Flarsheim et al. 1986).

Figure 5 (D) and 5 (E) show the cyclic voltammograms and the log-log plots of peak current versus scan rate obtained at MWCNTs/GC. It can be seen that at MWCNTs/GC electrode the oxidation potentials of HQ and CC shifted to the less positive potentials and the peak-peak separations were much reduced, indicating the oxidation processes possibly become apparently more electrochemically-reversible at the MWCNT surface. However a significant increase in the current responses is also observed. The slopes of the log-log plots were found to be 0.69 for the voltammograms of HQ and 0.70 for the voltammograms of CC. The observed slope values neither correspond to the value of 0.5, expected for the semi-infinite planar diffusion of the electroactive species, nor the value of 1.0 reflecting the occurrence of pure ‘thin-layer’ diffusion (Henstridge et al. 2010; Keeley and Lyons 2009; Sims et al. 2010; Streeter et al. 2008) or adsorptive voltammetry. Instead the slope values are likely to suggest the electrochemical behaviour of HQ and CC is a mix of semi-infinite planar diffusion in the

solution and diffusion within the layer coupled with ‘thin-layer’ effects and/or the adsorption within MWCNT layers. The significant contribution of the latter was also indicated by the observed large current increase. The transition from planar diffusion to ‘thin-layer’ diffusion can also cause the decreases in peak-peak separations and the shifts of peak oxidations seen in Figure 5 (D) and 5 (E), facilitating the differentiation of the signals from each other in a mixture of HQ and CC (Henstridge et al. 2010; Streeter et al. 2008). In particular the effect of thin layer diffusion is to shift the voltammetric signal to being close to the formal reversible potential of the couple under study and the voltammetric data shown in Figure 5 (D) and 5 (E) suggests a difference of ca. 110 mV in the values for CC and HQ.

Attempts to usefully resolve the voltammetric signals from mixtures of HQ and CC using SCV at a bare GC electrode or at a SPE-CNT were unsuccessful (Figure S6) so the SCV technique was next applied to enhance the sensitivity of detection via the use of MWCNT/GC electrodes.

### 2.2.2 Simultaneous determination of HQ and CC at a MWCNTs/GC

The analytical response of mixtures containing 5- 500 mM concentrations of HQ or CC were investigated using LSV, DPV and SCV, similar to section 2.1.2. The mixed solutions were prepared by standard additions of HQ or CC to obtain the concentration range of 5-500  $\mu\text{M}$  in the mixtures. The resulting voltammograms at MWCNTs/GC are shown in Figure 6 (A)-(C) and S7-S9. Figure 6 (A) compares linear sweep, differential pulse and semi-circular voltammograms of 500  $\mu\text{M}$  HQ+CC 1:1 mixture recorded at MWCNTs/GC at the same average scan rate of 50  $\text{mVs}^{-1}$ . As discussed in 2.1.2, in semi-circular voltammogram, the peaks can be selectively amplified when the  $E_{\text{mid}}$  of the applied potential window was shifted closer to the corresponding oxidation potentials. Semi-circular voltammetric measurements were made on 500  $\mu\text{M}$  HQ+CC 1:1 mixture using potential windows with varying  $E_{\text{mid}}$  (Figure S7).



As shown in Figure 6 (A)-(C),  $E_{\text{mid}}$  was adjusted to -0.10 V vs SCE and to 0.35 V vs SCE, for the separate selective determination of HQ and CC, respectively, where the optimal resolutions of both HQ and CC signals with selective amplifications were obtained. Under the chosen SCV potential window for HQ, the HQ oxidation peak was observed at 0.07 V vs SCE and is significantly larger in size than the CC oxidation peak observed at 0.17 V vs SCE. The additional peak at  $E_{\text{mid}}$  arises from capacitive currents which are largest when the instantaneous sweep rate is greatest. Similarly under the SCV when the potential window is suitably optimised for CC the relative sizes of HQ and CC peaks are reversed and the CC oxidation peak at 0.17 V vs SCE is enhanced. It can be seen that from Figure 6 (A) overall good resolutions were obtained via all three voltammetric techniques owing to the merit of using the MWCNTs/GC electrode, as discussed in 2.2.1. In comparison to LSV and SCV, DPV resulted in broader peaks but offers large peak currents due to the large extent of apparent reversibility in the present reaction system.

The linear ranges and sensitivities of the simultaneous detections of HQ and CC in their mixtures are compared as shown in Table S2. The calibration curve expressions of  $I_p$ -[HQ] and  $I_p$ -[CC] suggest that in the cases of both HQ and CC, linear range of 5-500 mM were found using LSV and SCV. SCV offers the more favourable sensitivity due to the selective amplification of the oxidation peaks of HQ and CC under the different potential windows. It is evident that SCV is particularly useful in sensitivity enhancement for system showing full or partial thin-layer voltammetry where the peak currents scale linear with scan rate rather than the square root of scan rate as for semi-infinite diffusive voltammetry leading to a larger relative sensitivity for SCV under these conditions.

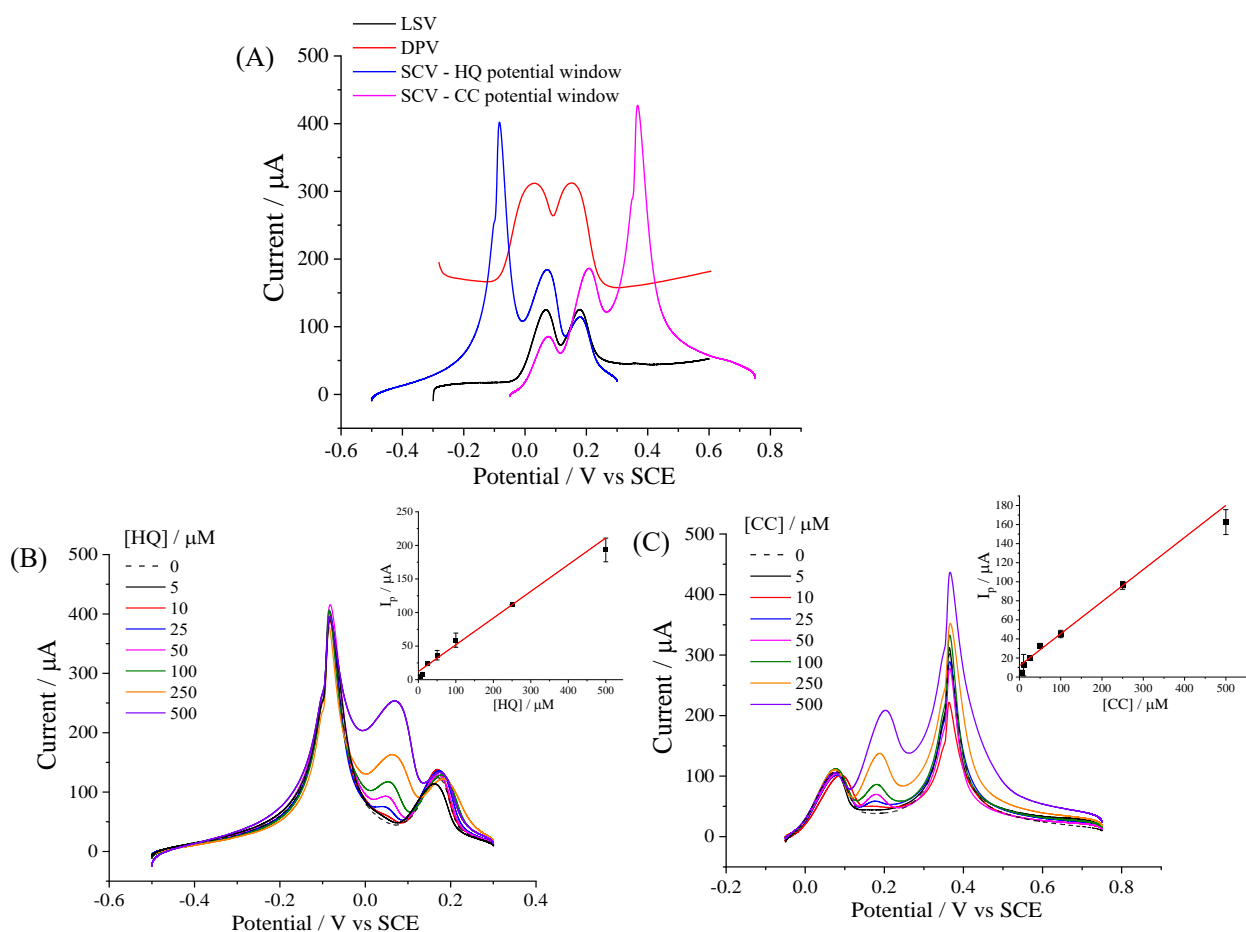


Figure 6. (A) Linear, differential pulse and semi-circular voltammetric responses of 500  $\mu\text{M}$  HQ+CC 1:1 mixture. Semi-circular voltammetric responses of (B) 5-500  $\mu\text{M}$  HQ in the presence of 500  $\mu\text{M}$  CC (C) 5-500  $\mu\text{M}$  CC in the presence of 500  $\mu\text{M}$  HQ at MWCNTs/GC electrode. The average scan rate applied in all voltammograms were 50  $\text{mV s}^{-1}$ . For SCV, the HQ potential windows was centred at -0.10 V vs. SCE and the CC potential window was centred at 0.35 V vs. SCE. The scan amplitude applied in (A)-(C) was 0.4 V. Insets of (B) and (C): plots of subtracted peak currents obtained from semi-circular voltammograms versus (B) HQ and (C) CC concentration.

In the developed method, MWCNTs/GC was used to distinguish the mixtures of HQ and CC, the isomers oxidised at very similar potentials, in combination with the employment of SCV which reinforced the resolutions of the voltammograms and improved the sensitivity of detection ca. 1.6 times from using conventional LSV in the concentration range of 5-500  $\mu\text{M}$ .

### 3. Conclusions

We have shown the value of using the novel voltammetric method of SCV for use in the electroanalysis of mixtures of ascorbic acid / acetaminophen, hydroquinone / catechol, and in S6 of the supporting information, glucose / ethanol. Compared to other conventional analytical voltammetries, LSV, DPV and DPV, SCV shows a significant advantage for the selective detections of the species in the model systems in the following two aspects. First, SCV resolves signals that are strongly-overlapped and are not distinguished using other voltammetries, offering the best possible voltammetric resolution amongst the methods compared. Second, SCV amplifies its peak current thus improving the sensitivity of detection. Using SCV at unmodified GC, Ni or MWCNTs dropcasted GC electrodes for the simultaneous detection of species in each of the above analytical system improves the analytical performance over the conventional methods, serving as a simple and accurate alternative to the existing electrochemical methodology without resort to elaborate electrode modification and/or strict experimental conditions.

## References:

- Ahammad, A.J.S., Akter, T., Mamun, A.A., Islam, T., Hasan, M.M., Mamun, M.A., Faraezi, S., Monira, F.Z., Saha, J.K., 2018. *J. Electrochem. Soc.* 165(9), B390-B397.
- Bosch, M.E., Sánchez, A.J.R., Rojas, F.S., Ojeda, C.B., 2006. *J Pharm Biomed Anal* 42(3), 291-321.
- Brett, C.M.A., Brett, A.M.O., 1993. Oxford University Press, Oxford; New York.
- Burestedt, E., Narvaez, A., Ruzgas, T., Gorton, L., Emnéus, J., Domínguez, E., Marko-Varga, G., 1996. *Anal. Chem.* 68(9), 1605-1611.
- Compton, R.G., Banks, C.E., 2018. *Understanding voltammetry*, third ed. World Scientific Publishing Europe, London.
- Enache, T.A., Oliveira-Brett, A.M., 2011. *J. Electroanal. Chem.* 655(1), 9-16.
- Ensafi, A.A., Rezaei, B., Zare, S.Z.M., Taei, M., 2010. *Sens Actuators B* 150(1), 321-329.
- Flarsheim, W.M., Tsou, Y.M., Trachtenberg, I., Johnston, K.P., Bard, A.J., 1986. *J. Phys. Chem.* 90(16), 3857-3862.
- Gojny, F.H., Nastalczyk, J., Roslaniec, Z., Schulte, K., 2003. *Chem. Phys. Lett.* 370(5), 820-824.
- Henstridge, M.C., Dickinson, E.J.F., Aslanoglu, M., Batchelor-McAuley, C., Compton, R.G., 2010. *Sens. Actuators B* 145(1), 417-427.
- Hu, F., Chen, S., Wang, C., Yuan, R., Yuan, D., Wang, C., 2012. *Anal. Chim. Acta.* 724, 40-46.
- Hu, I.F., Kuwana, T., 1986. *Anal. Chem.* 58(14), 3235-3239.
- Keeley, G.P., Lyons, M.E.G., 2009. *Int. J. Electrochem. Sc.* 4(6), 794-809.
- Kitagawa, Y., Kitabatake, K., Suda, M., Muramatsu, H., Ataka, T., Mori, A., Tamiya, E., Karube, I., 1991. *Anal. Chem.* 63(20), 2391-2393.
- Molina, Á., González, J., 2016. *Pulse Voltammetry in Physical Electrochemistry and Electroanalysis Theory and Applications*, first ed. Springer.
- Nematollahi, D., Shayani-Jam, H., Alimoradi, M., Niroomand, S., 2009. *Electrochim. Acta* 54(28), 7407-7415.
- Padayatty, S.J., Katz, A., Wang, Y., Eck, P., Kwon, O., Lee, J.-H., Chen, S., Corpe, C., Dutta, A., Dutta, S.K., Levine, M., 2003. *J. Am. Coll. Nutr.* 22(1), 18-35.
- Pandey, R.R., Alshahrani, H.S., Krylyuk, S., Williams, E.H., Davydov, A.V., Chusuei, C.C., 2018. *Electroanal.* 30(5), 886-891.
- Ribeiro, A.C.F., Barros, M.C.F., Veríssimo, L.M.P., Santos, C.I.A.V., Cabral, A.M.T.D.P.V., Gaspar, G.D., Esteso, M.A., 2012. *J. Chem. Thermodyn.* 54, 97-99.
- Rice, R., Allred, C., McCreery, R., 1989. *J. Electroanal. Chem.* 263(1), 163-169.
- Robinson, D., Anderson, J.E., Lin, J.L., 1990. *J. Phys. Chem.* 94(2), 1003-1005.
- Săndulescu, R., Mirel, S., Oprean, R., 2000. *J. Pharm. Biomed. Anal.* 23(1), 77-87.
- Shkotova, L.V., Piechniakova, N.Y., Kukla, O.L., Dzyadevych, S.V., 2016. *Food Chemistry* 197, 972-978.
- Sims, M.J., Rees, N.V., Dickinson, E.J.F., Compton, R.G., 2010. *Sens. Actuators B* 144(1), 153-158.
- Streeter, I., Wildgoose, G.G., Shao, L., Compton, R.G., 2008. *Sens Actuators B* 133(2), 462-466.
- Uchida, Y., Kätelhön, E., Compton, R., 2019a. *J. Electroanal. Chem.* 848, 113290.
- Uchida, Y., Katelhon, E., Compton, R.G., 2018a. *J. Electroanal. Chem.* 823, 465-473.
- Uchida, Y., Katelhon, E., Compton, R.G., 2018b. *J. Electroanal. Chem.* 818, 140-148.
- Uchida, Y., Katelhon, E., Compton, R.G., 2019b. *J. Electroanal. Chem.* 835, 60-66.
- Uchida, Y., Kätelhön, E., Compton, R.G., 2017. *J. Electroanal. Chem.* 801, 381-387.
- Uchida, Y., Kätelhön, E., Compton, R.G., 2018c. *J. Electroanal. Chem.* 810, 135-144.
- Wang, J., 2006. *Analytical electrochemistry*, third ed. Wiley-VCH, Hoboken.
- Wang, Y., Chen, L., Compton, R.G., 2020. *Food Chemistry* 323, 126844.
- Wang, Y., Compton, R.G., 2020. *ChemElectroChem* 7(16), 3508-3516.
- Wang, Z., Li, S., Lv, Q., 2007. *Sens. Actuators B* 127(2), 420-425.
- Wilson, R., Turner, A.P.F., 1992. *Biosens. Bioelectrons.* 7(3), 165-185.
- Xie, T., Liu, Q., Shi, Y., Liu, Q., 2006. *J. Chromatogr. A* 1109(2), 317-321.
- Xiong, L., Compton, R.G., 2014. *Int. J. Electrochem. Sc.* 9(12), 7152-7181.
- Yue, X., Pang, S., Han, P., Zhang, C., Wang, J., Zhang, L., 2013. *Electrochem. commun.* 34, 356-359.
- Zhao, D., Zhang, X., Feng, L., Jia, L., Wang, S., 2009. *Colloids. Surf B* 74(1), 317-321.