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PAPER

A green approach to Fenton chemistry: mono-hydroxylation of salicylic acid in aqueous medium by the electrogeneration of Fenton's reagent†

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First, the electrochemical characteristics of Fenton's reagent (Fe(III), Fe(II) and hydrogen peroxide), including its catalytic (EC′) behaviour were investigated. Second, the electrogeneration of hydrogen peroxide by a two-electron reduction of dissolved oxygen was conducted at a carbon electrode in a divided electrolysis cell and the concentration of hydrogen peroxide obtained was determined by the titration. The two approaches were then combined to give a one-pot, relatively green approach to aromatic hydroxylation reactions, with the electro-Fenton method allowing the iron to be used catalytically and the oxygen/water employed as the hydroxylation reagent by the *in situ* production of hydrogen peroxide. In particular, the preparative-scale hydroxylation of salicylic acid has been studied in an oxygen-saturated 0.1 M Na_2SO_4 pH 3.0 solution containing 5 mM Fe(II) and 5 mM salicylic acid at the controlled potential of −1.0 V *vs.* SCE. The study showed that after the attack of the hydroxyl radical produced *in situ* by the electro-Fenton process on salicylic acid, 2,3- and 2,5-dihydroxybenzoic acids were detected as primary monohydroxylated products with the highest yield of *ca.* 21.6 ± 2.5%.

1. Introduction

Advanced oxidation processes (AOPs) have been widely used for the treatment of wastewater containing organic contaminants such as pesticides, surfactants, colouring matters and pharmaceuticals that are difficult to degrade.[1–8] The main mechanism of AOPs are based on the generation of hydroxyl radical ($^{\bullet}OH$), a very powerful oxidant capable of rapidly reacting with organic compounds yielding dehydrogenated or hydroxylated derivatives until achieving their complete mineralization (*i.e.* conversion into carbon dioxide, water and inorganic ions).[1–9] In AOPs, the $^{\bullet}OH$ radical can be obtained from Fenton (Fe(II)/H_2O_2, first studied by H. J. H. Fenton[10] in 1894) and/or Fenton-like (Fe(III)/H_2O_2) processes which have been extensively reported in the literature.[1–18] Generally, the Fenton system consists of ferrous ions mixed with hydrogen peroxide under acidic conditions (pH ranging from 2–4), generating the $^{\bullet}OH$ radical, a powerful oxidizing intermediate as shown in eqn (1).[6–18]

$$Fe^{2+} + H_2O_2 \rightarrow {}^{\bullet}OH + {}^{-}OH + Fe^{3+} \qquad (1)$$

Although the reaction involves the consumption of one molecule of Fe(II) for each $^{\bullet}OH$ radical produced, Fe(II) catalysts can be regenerated in the system through the reaction of Fe(III) with H_2O_2 (Fenton-like-reaction) shown in eqn (2).[5–7,12–15]

$$Fe^{3+} + H_2O_2 \rightarrow Fe^{2+} + {}^{\bullet}OOH + H^{+} \qquad (2)$$

According to the mechanism above (eqn (1) and (2)), it can be seen that the iron in Fenton and Fenton-like reactions cycles between the Fe(II) and Fe(III) oxidation states. However, the reduction of Fe(III) is generally slower than the oxidation Fe(II),[19] hence the amounts of Fe(II) and hydrogen peroxide used in Fenton process to generate hydroxyl radical are often greater than the stoichiometric quantities of aromatic contaminants.[3,15,20,21] The main drawbacks of this technique involve the high price of commercial hydrogen peroxide and the operational costs associated with safe handling and transportation of hydrogen peroxide and maintaining the correct concentration of this compound throughout a reaction.[12,18] In particular, the decomposition of hydrogen peroxide can occur rapidly when it has been exposed to sunlight or certain metallic impurities and enzymes, as shown in eqn (3).

$$2H_2O_2\ (aq) \rightarrow 2H_2O(l) + O_2\ (g) \qquad (3)$$

Recently, new advanced oxidation processes induced by electrochemistry have been studied and proposed as an alternative approach. These are known as electrochemical advanced oxidation

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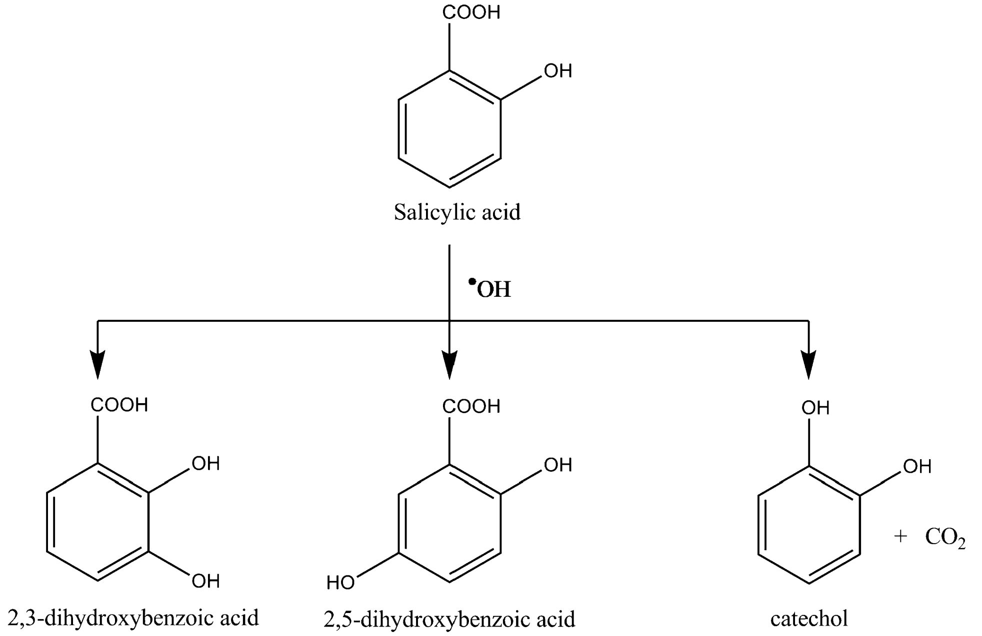


Scheme 1 Products of the attack of •OH radical on salicylic acid reported by Halliwell and Grootveld.[32,33]

processes (EAOPs).[3,5,7,18,22–26] Electrochemical methods are clean, environmentally friendly, versatile and effective techniques for the direct production (anodic oxidation) or indirect generation *via* Fenton's reagent (electro-Fenton approach) of the hydroxyl radical.[3,5,7,18,22–26] In anodic oxidation, the hydroxyl radical is generated as an intermediate and often remains adsorbed on a high O_2-overvoltage anode in a direct water oxidation process, as shown in eqn (4).

$$H_2O \rightarrow {}^{\bullet}OH_{(ads)} + H^+ + e^- \qquad (4)$$

In the electro-Fenton method, hydrogen peroxide is electrochemically generated *in situ* in acidic medium *via* the two-electron reduction of dissolved oxygen on the surface of a carbonaceous cathode, shown in eqn (5). It is interesting to note that oxygen is very cheap (less than £0.1 per 100 g),[27] abundant, and essentially risk-free, compared to the high cost (at least £10 per 100 mL)[28] and the difficulty in handling and storage of commercial hydrogen peroxide discussed earlier.

$$O_2\ (g) + 2H^+ + 2e^- \rightarrow H_2O_2 \qquad (5)$$

The electrogenerated hydrogen peroxide can be catalytically transformed to hydroxyl radicals by means of ferrous ions as in eqn (1). Hydroxyl radicals formed by the Fenton process can then act as powerful oxidising agents for the complete mineralisation of aromatic compounds,[3–7,15,20,21,23] including pharmaceuticals such as salicylic acid in wastewater.

Salicylic acid (2-hydroxybenzoic acid) is widely used in cosmetics and pharmaceuticals.[3,15,20,21,29,30] It is a key ingredient in many skin-care products for the treatment of acne, corns and warts due to its distinct exfoliating, antiseptic and anti-inflammatory properties.[15,20] It is also a primary hydrolysate of acetylsalicylic acid (aspirin) which is commonly used as anti-inflammatory medicine.[3,30]

In previous work regarding the mineralization of salicylic acid by chemical Fenton treatment, it has been reported that the concentration of hydrogen peroxide significantly influenced the degradation of salicylic acid.[15,20] Relatively high molar ratios of H_2O_2 to salicylic acid and Fe(II) were favourable. Complete degradation of salicylic acid was achieved within 1–2 min when the molar ratio of H_2O_2 to salicylic acid was 4 : 1.[20] Moreover, it has been demonstrated that salicylic acid was rapidly mineralised by •OH radical generated from Fenton's reaction *via* the main reaction intermediates of 2,3-dihydroxybenzoic, 2,5-dihydroxybenzoic and 2,6-dihydroxybenzoic acids.[3,21] These intermediates were oxidised further by •OH radical to, for example, α-ketoglutaric acid, glycolic acid, maleic acid, fumaric acid, malic acid, tartronic acid and finally to oxalic acid which could then form an Fe(III)-oxalate complex, indicating the complete degradation of salicylic acid. The proposed reaction sequence for salicylic acid mineralisation by •OH radical formed from Fenton's process was also reported.[3]

In addition, the use of Fenton chemistry for the hydroxylation of salicylic acid has previously been investigated, by the application of stoichiometric (or greater) quantities of Fenton reagents.[31,32] For example, Tomita *et al.*[31] reported that when salicylic acid, hydrogen peroxide and Fe(II) were mixed together, •OH radical was generated in the system and it then attacked salicylic acid to produce the major products of 2,3- and 2,5-dihydroxybenzoic acids with 2,3-dihydroxybenzoic acid being prominent. Note that various amounts of catechol, 2,4- and 2,6-dihydroxybenzoic acids were also observed when the concentration of Fe(II) was equal to or larger than that of hydrogen peroxide. Besides, Halliwell and Grootveld[32,33] also reported that after the attack of •OH radical on salicylic acid, three products namely 2,3-dihydroxybenzoic acid (*ca.* 49%), 2,5-dihydroxybenzoic acid (*ca.* 40%) and catechol (*ca.* 11%), can be detected, as illustrated in Scheme 1.

As highlighted in the literature,[32,33] the attack of •OH radical on salicylic acid produces 2,3-dihydroxybenzoic acid and 2,5-dihydroxybenzoic acid as major products, suggesting that the formation of these two dihydroxybenzoic acids could be applied as a responsive assay for •OH radical formation. Indeed, aromatic hydroxylation has been previously used as a method for measuring the production of •OH radical both *in vitro* and *in vivo*.[32–34]

In this work, the electrochemical characteristics of Fe(III) in the presence of either hydrogen peroxide (Fenton's reagent) or salicylic acid are investigated. Furthermore, the electrogeneration of hydrogen peroxide from oxygen reduction is performed in aqueous media by controlled-potential coulometry, and the concentration of *in situ* hydrogen peroxide produced is then determined by the titration. Finally, the application of the electro-Fenton method with simultaneous hydrogen peroxide electrogenerated *in situ* for the mono-hydroxylation of salicylic acid, representative of soluble aromatic compounds, yielding the products of 2,3- and 2,5-dihydroxybenzoic acids, is first reported and discussed here.

2. Experimental

2.1 Reagents and equipment

Iron(III) sulphate pentahydrate ($Fe_2(SO_4)_3{\cdot}5H_2O$, 97%), and iron(II) sulphate heptahydrate ($FeSO_4{\cdot}7H_2O$, 98%) were purchased from Sigma-Aldrich (Gillingham, UK). Salicylic acid, sodium salt ($2\text{-}(HO)C_6H_4CO_2Na$, 99%) was supplied by BDH (Poole, UK). All other chemicals were purchased from Sigma-Aldrich (Gillingham, UK). All the reagents were used without further purification. All solutions were prepared using deionised water of resistivity not less than 18.2 MΩ cm^{-1} at 298 ± 2 K (Millipore UHQ, Vivendi, UK).

Sonication was carried out using a D-78224 Singen/Htw sonicator (50/60 Hz, 80 W, UK). pH measurement was made using a pH213 pH meter (Hanna instrument, UK).

Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Bruker Avance AV400 spectrometer (400 MHz) at the Chemical Research Laboratory, Department of Chemistry, University of Oxford, UK, in DMSO-d_6 and referenced to the residual solvent peak and integrated relative to cyclohexene as an internal standard. Chemical shifts are quoted in ppm (parts per million) to the nearest 0.01 ppm with signal splittings recorded as singlet (s), doublet (d) and triplet (t). ^1H NMR spectra were recorded at room temperature.

Electrochemical measurements were recorded using an Autolab PGSTAT 20 computer-controlled potentiostat (EcoChemie, Utrecht, The Netherlands) with a standard three-electrode configuration. A glassy carbon electrode (GC, 3.0 mm diameter, BAS Technical, UK) was used as the working electrode. A saturated calomel electrode (SCE) and a carbon rod acted as the reference and counter electrodes respectively. The GC was polished using diamond pastes of decreasing sizes (Kemet, UK). Cyclic voltammetry was recorded at a scan rate of 50 mV s^{-1}, except where stated. Bulk electrolysis was performed in a divided electrolysis cell that consisted of a reticulated vitreous carbon (RVC) working electrode, a platinum wire (Pt) counter electrode and a reference electrode, SCE. All electrochemical experiments were carried out at room temperature in 0.1 M sodium sulphate solution (pH 3.0).

2.2 Titration of hydrogen peroxide by $KMnO_4$

The simplest and most commonly used method for the determination of hydrogen peroxide is by titration with potassium permanganate ($KMnO_4$).[35–37] Potassium permanganate is a strong oxidising agent that can quantitatively react with hydrogen peroxide acidified with diluted sulphuric acid as shown below in eqn (6) (in net ionic form).[35–37]

$$2MnO_4^- + 5H_2O_2 + 6H^+ \rightarrow 2Mn^{2+} + 5O_2 + 8H_2O \quad (6)$$

Potassium permanganate is intensely purple, even at very low concentration, while manganous ion (Mn^{2+}) is colourless, therefore, there is no need to use an indicator to indicate the

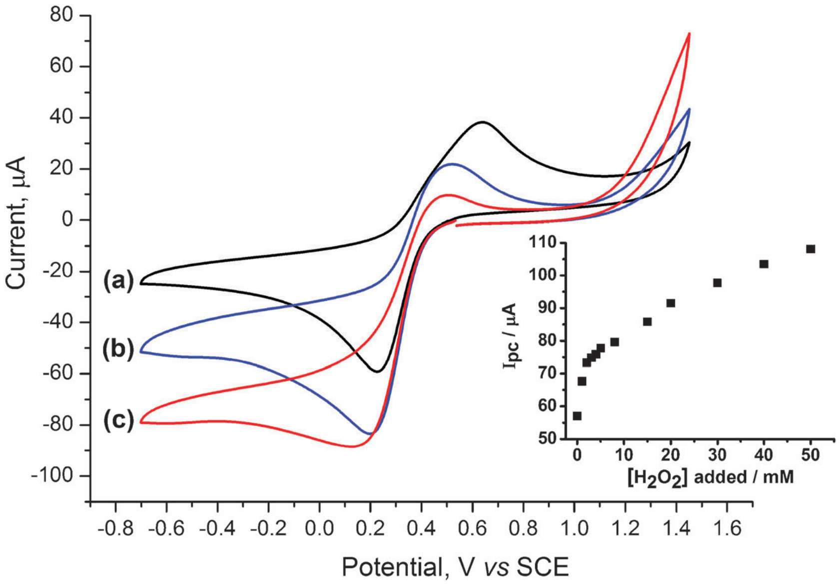


Fig. 1 Overlaid cyclic voltammograms of 5 mM Fe(III), recorded at a glassy carbon (GC) electrode, in the absence (a) and presence of 5 mM (b) and 10 mM (c) H_2O_2, in 0.1 M Na_2SO_4 pH 3.0. All scans at 50 mV s^{-1}. Inset: Plot of cathodic peak current (I_{pc}) *vs.* concentration of H_2O_2 (0, 1, 2, 3, 4, 5, 8, 15, 20, 30, 40 and 50 mM) added.

end point of the reaction as it is self-indicating.[36] Further details of the titration of hydrogen peroxide by potassium permanganate can be found in the Supporting Information† (Section I).

3. Results and discussion

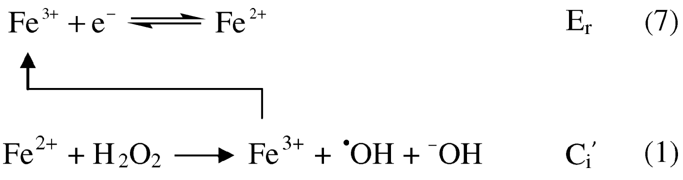
3.1 Voltammetric behaviour of Fe(III) in the presence of H_2O_2

The behaviour of Fe(III) in the presence of hydrogen peroxide was first investigated. Fig. 1 displays the overlaid cyclic voltammograms of 5 mM Fe(III) in the absence (a) and presence of 5 mM (b) and 10 mM (c) H_2O_2 in 0.1 M Na_2SO_4 pH 3.0, measured at 50 mV s^{-1}. As illustrated in Fig. 1a, the redox couple of Fe(III)/Fe(II) was observed with the cathodic peak potential of *ca.* +0.22 V *vs.* SCE. The ratio of anodic peak current (I_{pa}) to cathodic peak current (I_{pc}) was found to be close to one, indicating a quasi-reversible one-electron transfer process, as shown in eqn (7).[38,39]

$$Fe^{3+}\,(aq) + e^- \rightleftharpoons Fe^{2+}\,(aq) \qquad (7)$$

A scan rate study between 10 to 200 mV s^{-1} (shown in Fig. 2) demonstrated that the cathodic peak current (I_{pc}) was linear with respect to the square-root of scan rate (●, plotted as an inset in Fig. 2). This result showed that the electrode process is diffusion controlled.[38,39] Similar electrochemical behaviour of Fe(III)/Fe(II) redox couple has been previously reported in the literature.[40]

Next, when hydrogen peroxide (in 5 mM Fe(III)) was added to a 5 mM Fe(III) solution (Fig. 1b and c), a response consistent with an electrochemical catalytic cycle could be observed. Upon the addition of H_2O_2, the cathodic peak current (I_{pc}) increased in height while the anodic peak for the oxidation of Fe(II) became smaller, due to the chemical consumption of Fe(II) by H_2O_2 corresponding to the catalytic (EC′) reaction.[38,39] In the catalytic reaction scheme, hydrogen peroxide reacts in the following chemical reaction to regenerate Fe(III), as shown earlier in eqn (7) and (1).



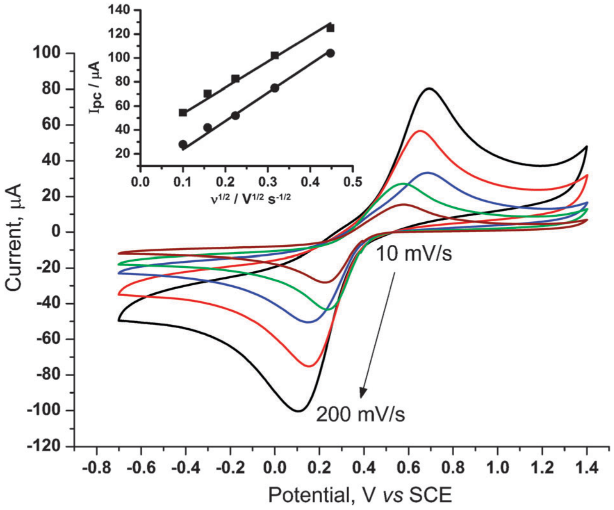


Fig. 2 Overlaid cyclic voltammograms of scan rate study (10–200 mV s^{-1}) for 5 mM Fe(III) in 0.1 M Na_2SO_4 pH 3.0, recorded at a glassy carbon (GC) electrode. Inset: Plot of cathodic peak current (I_{pc}) *vs.* square-root of scan rate ($\nu^{1/2}$) at a GC electrode for 5 mM Fe(III) itself (●, $R^2 = 0.998$) and 5 mM Fe(III) in the presence of 10 mM H_2O_2 (■, $R^2 = 0.999$).

Previously, several studies have investigated the reaction between iron catalysts and hydrogen peroxide ("Fenton's reagent") and its mechanism is also well-studied in the literature.[1–3,7,12,13] In brief, Fe(II) commonly used in the Fenton process reacts chemically with H_2O_2, yielding ${}^\bullet OH$ radical and Fe(III) as shown above in eqn (1).

According to the Fe(II)/H_2O_2 Fenton process, the voltammetric response of Fe(III) combined with H_2O_2 obtained in this study confirms that after the electrochemical reduction of Fe(III), hydrogen peroxide was catalytically reduced by electrogenerated Fe(II). With the EC′ mechanism, Fe(III) was continuously regenerated by the coupled chemical reaction, resulting in the increase in cathodic peak current (I_{pc}), as shown in Fig. 1. In Fe(III) solutions containing a large excess of hydrogen peroxide, the cathodic peak current (I_{pc}) grew with the concentration of hydrogen peroxide (plotted as an inset in Fig. 1) in a manner expected by EC′ process.[38,39]

A scan rate study of 5 mM Fe(III) in the presence of 10 mM H_2O_2 was examined and the resulting voltammograms are shown in Fig. 3. It can be seen that the anodic peak current (I_{pa}) corresponding to the oxidation of Fe(II) increased with increasing scan rates as there was less effect of chemical reaction involved at high scan rates.[38,39] A plot of cathodic peak current (I_{pc}) *vs.* square-root of scan rate (■, plotted as an inset in Fig. 2) shows a linear response; however, it does not go through the origin, which is consistent with the EC′ process suggested.

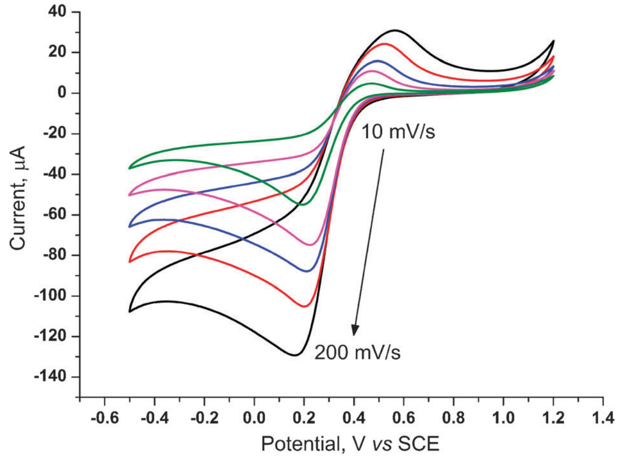


Fig. 3 Overlaid cyclic voltammograms of scan rate study (10–200 mV s^{-1}) for 5 mM Fe(III) in the presence of 10 mM H_2O_2, in 0.1 M Na_2SO_4 pH 3.0, recorded at a glassy carbon (GC) electrode.

3.2 Voltammetric behaviour of Fe(III) in the presence of salicylic acid

Fig. 4 displays typical cyclic voltammograms of (a) 5 mM Fe(III), (b) 5 mM salicylic acid and (c) 5 mM Fe(III) in the presence of 5 mM salicylic acid, in 0.1 M Na_2SO_4 pH 3.0. Fig. 4a shows the reduction of Fe(III), whereas Fig. 4b represents the direct oxidation of salicylic acid. Note that for the latter process, an irreversible anodic peak (I_a) was observed only in the first anodic scan, with a peak potential at *ca.* 1.06 V *vs.* SCE. As previously reported in the literature,[30,41–43] this anodic peak can be used for direct electroanalytical determination of salicylic acid. On the reverse scan, no reverse reduction peak for salicylic acid was observed, suggesting an oxidation process followed by a fast irreversible chemical reaction, which rapidly removed the generated product.[30,38,44] Moreover, it was found that the oxidation peak current for salicylic acid noticeably decreased in the second scan as the electrode was passivated. The literature contains various reports of the electrochemical oxidation of phenols and substituted phenols in aqueous solution.[29,30,44] When the concentration of phenolic compounds was higher than 0.5 mM, electrode passivation is observed after a single voltammetric scan, caused by the formation of polymer films on the electrode surface.[29,30,44]

When an equimolar concentration of salicylic acid (in 5 mM Fe(III)) was added to a 5 mM Fe(III) solution, the colour of the solution changed from pale yellow to violet as a result of the formation of intensely coloured complexes between salicylic acid and Fe(III).[20,45] The reaction between Fe(III) and salicylic acid under acidic conditions, leading to the formation of a 1 : 1 and/or 1 : 2 stable complex, has been previously reported in the literature and shown in eqn (8) and (9).[20,45–47] In contrast, no absorption spectrum in the range of 400–600 nm could be observed for the Fe(II)-salicylic acid complex when 5 mM of Fe(II) and salicylic acid were mixed, suggesting little, if any, complexation occurred, at least at the concentration studied.[46]

$$Fe^{3+} + C_7H_6O_3 \rightarrow [FeC_7H_4O_3]^+ + 2H^+ \qquad (8)$$

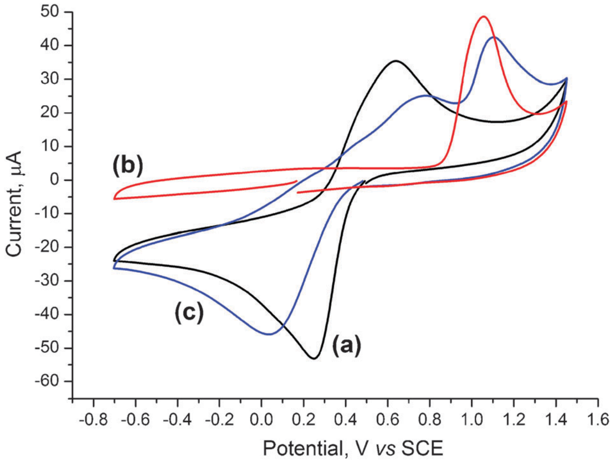


Fig. 4 Overlaid cyclic voltammograms of (a) 5 mM Fe(III), (b) 5 mM salicylic acid and (c) 5 mM Fe(III) in the presence of 5 mM salicylic acid, in 0.1 M Na_2SO_4 pH 3.0, recorded at a glassy carbon (GC) electrode, at 50 mV s^{-1}.

$$Fe^{3+} + 2(C_7H_6O_3) \rightarrow [Fe(C_7H_5O_3)_2]^+ + 2H^+ \qquad (9)$$

The cyclic voltammetric behaviour of Fe(III)-salicylic acid complex was also investigated. As seen in Fig. 4c, one cathodic peak corresponding to the reduction of Fe(III) could be observed at *ca.* 0.21 V (*vs.* SCE) more negative than that for Fe(III) alone, owing at least in part to the fact that a stable Fe(III)-salicylic acid complex is thermodynamically more difficult to reduce than free Fe(III). In addition, the anodic counterpart of that cathodic peak shifted towards more positive values and the peak became very small and ill-defined. Another anodic peak was also observed at *ca.* 1.11 V *vs.* SCE, with a slight shift in potential towards the positive direction when compared to salicylic acid itself. It should be noted that the redox couple of Fe(III)/Fe(II) disappeared after the first cathodic scan, while the second irreversible oxidation peak got smaller with the cycle numbers, suggesting the passivation of the electrode surface as described earlier.

A scan rate study of 5 mM Fe(III) in the presence of 10 mM salicylic aicid was further investigated and is shown in Fig. 5. The anodic peak current (I_{pa}) corresponding to the oxidation of salicylic acid increased linearly with scan rate (plotted as an inset in Fig. 5), and not with respect to the square root of scan rate, demonstrating that the process of electrode reaction is largely controlled by adsorption of the Fe(III)-salicylic acid complex(s) at the carbon surface.

3.3 *In situ* electrochemical generation of H_2O_2

The reduction of oxygen was initially investigated in a small ratio of electrode surface area (A) to the volume of the solution (V) condition using a bare glassy carbon (GC) electrode in order to confirm its performance characteristics (*e.g.* reduction potential of oxygen) before bulk electrolysis was performed. Fig. 6 displays the typical cyclic voltammograms of an oxygen-saturated (solid line) and an oxygen-free (dashed line) 0.1 M Na_2SO_4 pH 3.0 solution. As can be seen from Fig. 6, for

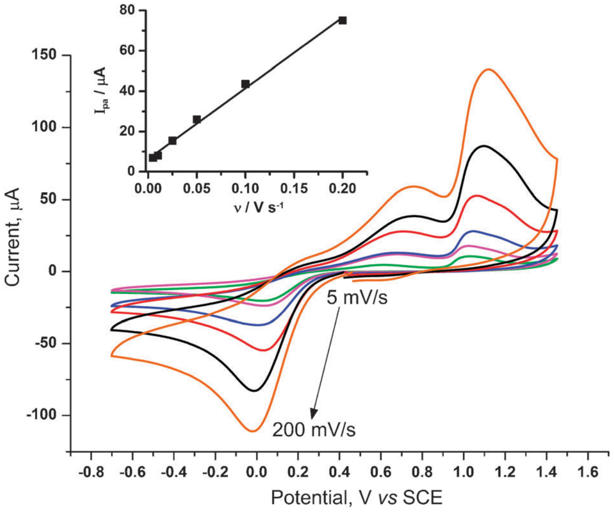


Fig. 5 Overlaid cyclic voltammograms of scan rate study (5–200 mV s^{-1}) for 5 mM Fe(III) in the presence of 10 mM salicylic acid, in 0.1 M Na_2SO_4 pH 3.0, recorded at a glassy carbon (GC) electrode. Inset: Plot of anodic peak current (I_{pa}) corresponding to the oxidation of salicylic acid *vs.* scan rate (ν), with correlation coefficient (R^2) = 0.994.

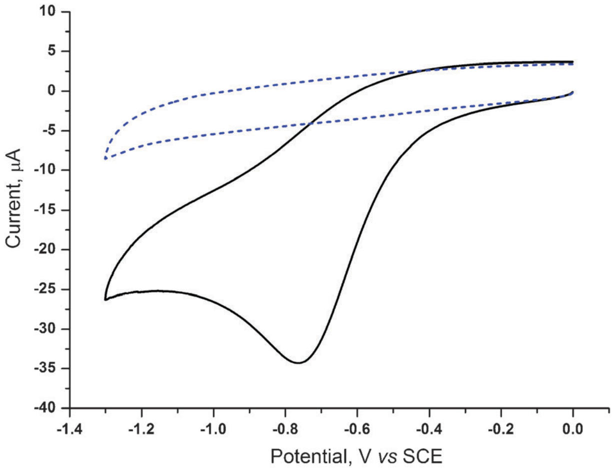


Fig. 6 Overlaid cyclic voltammograms for a bare glassy carbon (GC) electrode, recorded in an O_2-saturated (solid line) and a N_2-saturated (dashed line) Na_2SO_4 0.1 M pH 3.0 solution, at 50 mV s^{-1}.

an oxygen-saturated solution, a large irreversible reduction peak was observed at *ca.* −0.75 V *vs.* SCE, while no obvious voltammetric peak could be seen in the absence of oxygen. These voltammetric results correspond to the two-proton-two-electron reduction of oxygen, leading to the formation of hydrogen peroxide,[23] as shown in eqn (5).

Potentiostatic electrolysis was subsequently conducted in order to determine whether oxygen could be successfully electrolysed to produce hydrogen peroxide. In summary, controlled-potential coulometry was performed in a 10.00 mL of oxygen-saturated 0.1 M Na_2SO_4 pH 3.0 solution at −1.0 V *vs.* SCE in a divided electrolysis cell using a reticulated vitreous carbon (RVC) electrode as a working electrode. The electrolysis solution was thoroughly stirred during the reaction by continuous bubbling of oxygen gas. The total number of coulombs (Q) consumed in each electrolysis was monitored and deliberately set to be 2.41 C, 4.82 C, 7.24 C and 9.65 C. According to Faraday's law, the amount of oxygen electrolysed in each electrolysis (which is theoretically in 1 : 1 stoichiometric ratio of hydrogen peroxide formed) can be calculated by using eqn (10):[38]

$$Q = nFN \qquad (10)$$

where Q represents the total amount of charge passed in the electrolysis (C); n is the number of electrons involved in the reaction; F is the Faraday constant (C mol^{-1}) and N is the mole number of substrates that have been electrolysed (mol).

Based on Faraday's law, the concentration of hydrogen peroxide generated in a 10 mL of electrolysis solution with four different amounts of charge passed through (2.41 C, 4.82 C, 7.24 C and 9.65 C) could then be calculated and inferred to be 1.25 mM, 2.50 mM, 3.75 mM and 5.0 mM, respectively.

The hydrogen peroxide formed by the electrolysis process was next quantified by titration with potassium permanganate ($KMnO_4$),[36,37] detailed in Experimental section. Simply, 5.00 mL of each resulting hydrogen peroxide solution obtained from the electrolysis described above was first acidified with H_2SO_4 and subsequently titrated with $KMnO_4$. When $KMnO_4$ was added dropwise to an acidified solution of hydrogen peroxide, each drop was decolourised until all hydrogen peroxide was used up (reaction shown in eqn (6)). The next drop of $KMnO_4$ added coloured the solution, indicating the end-point of the titration. The actual content of hydrogen peroxide formed by the electrolysis process can then be determined.

Fig. 7 displays the plot of concentrations of hydrogen peroxide experimentally determined by the titration (solid line) against those theoretically calculated based on Faraday's law (dashed line). The experiments (either bulk electrolysis or titration) were performed in triplicate and the results were the average of three independent experiments. As shown in Fig. 7, the actual concentrations of hydrogen peroxide electrochemically generated *in situ* with four different amounts of charge consumed (2.41 C, 4.82 C, 7.24 C and 9.65 C) were found to be 1.21 mM, 2.30 mM, 3.60 mM and 4.23 mM, respectively. These experimental values agree with the theoretical data calculated earlier with the electrolysis current efficiency for *in situ* hydrogen peroxide formation of *ca.* 85–97%.

3.4 Bulk reaction of the electrogenerated •OH radical with salicylic acid

A preparative-scale hydroxylation of salicylic acid was next performed at −1.0 V *vs.* SCE in a divided electrolysis cell with a reticulated vitreous carbon (RVC) cathode in 10.00 mL of an oxygen-saturated 0.1 M Na_2SO_4 pH 3.0 solution containing 5 mM salicylic acid and 5 mM Fe(II). The electrolysis solution was thoroughly stirred during the reaction by continuous bubbling of oxygen gas. At a controlled potential of −1.0 V *vs.* SCE, hydrogen peroxide was first produced *in situ via* a two-electron O_2 reduction process, followed by a reaction with Fe(II), generating hydroxyl radical, hydroxide and Fe(III), as described earlier. Next, the *in situ* electrogenerated hydroxyl radical was expected to react with salicylic acid in the solution.[32,33] The total amount of charge (C) passed during each electrolysis was monitored and set to the exact values, shown in Table 1. It is important to note that apart from the two-electron reduction of O_2 to H_2O_2 taking place during the controlled-potential electrolysis, Fe(III), simultaneously generated

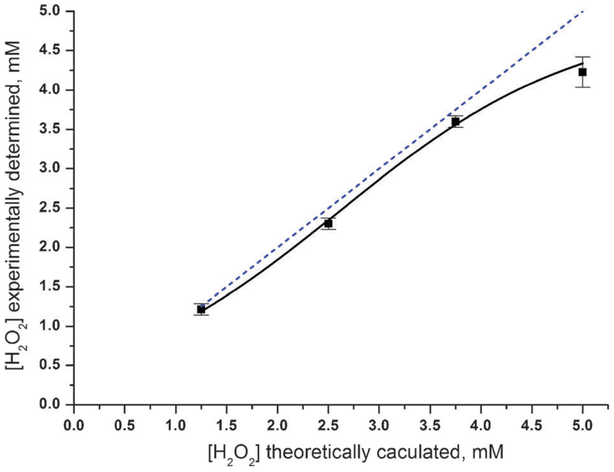


Fig. 7 Plot of H_2O_2 concentrations electrochemically generated *in situ* determined experimentally by titration (solid line) *versus* theoretically calculated from Faraday's law (dashed line).

Table 1 The total amount of charge (C) consumed in each bulk electrolysis of an O_2-saturated 0.1 M Na_2SO_4 pH 3.0 solution containing 5 mM salicylic acid and 5 mM Fe(II) with expected concentration of hydrogen peroxide (mM) electrogenerated *in situ* at −1.0 V *vs.* SCE, calculated from $Q = nFN$, based on a two-electron O_2 reduction process. Also shown is the estimated percentage of charge passed corresponding to a 1 : 1 stoichiometric reaction between 5 mM Fe(II) and H_2O_2 formed in the system

Amount of charge passed during each electrolysis (C)	Expected concentration of H_2O_2 formed *in situ* during electrolysis (mM)	Percentage of charge passed (%)
0	0	0
0.97	0.34	6.7
2.41	0.83	16.7
4.82	1.67	33.3
7.24	2.50	50.0
9.65	3.33	66.7
14.48	5.00	100.0

in the system by the reaction of H_2O_2 and Fe(II), could also accept one electron, being reduced to Fe(II). Considering the electric charge consumption in the two-electron O_2 reduction reaction, the concentration of hydrogen peroxide formed in the system could then be theoretically estimated based on Faraday's law (shown in Table 1). In addition, the percentage of charge passed in each electrolysis could be calculated by taking a 1 : 1 stoichiometric reaction between 5 mM Fe(II) and hydrogen peroxide formed *in situ* into account (shown in Table 1).

The resulting mixture at the end of each electrolysis was then acidified to pH 1 by the addition of aqueous 1.0 M HCl. The aqueous layer was next extracted with EtOAc (5 × 10 mL). The combined organics were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo* to give the product. The reaction products obtained from the electrolysed mixture before and after controlled potential electrolysis reaction were then analysed by proton nuclear magnetic resonance (^1H NMR) spectroscopy. As demonstrated in the Supporting Information† (Section II), four signals of protons could be observed in both cases at δ 6.95 ppm (dd, H-3 of salicylic acid), 7.51 ppm (td, H-4 of salicylic acid), 6.91 ppm (td, H-5 of salicylic acid) and 7.80 ppm (dd, H-6 of salicylic acid), corresponding to ^1H NMR spectrum of salicylic acid.[48–50] After the bulk reaction, additional proton signals for hydroxylated products namely 2,3- and 2,5-dihydroxybenzoic acids were observed, confirming the hydroxylation of salicylic acid by •OH radical electrogenerated *in situ via* electro-Fenton process. The signals at δ 7.24 ppm (dd, H-6 of 2,3-dihydroxybenzoic acid) and 7.15 ppm (d, H-6 of 2,5-dihydroxybenzoic acid) were used for analysis due to their position in an otherwise clear region of the spectrum.

In order to determine the total yield of these two monohydroxylated products, cyclohexene (–CH=CH–, δ 5.60 ppm, ^1H NMR not shown) was used as an internal standard. The conversion percentage of salicylic acid to its hydroxylated derivatives was obtained by comparing the integration of corresponding peaks in the product and starting material. Both signals were normalised with respect to the cyclohexene signal. Fig. 8 displays the percentage conversion of salicylic acid to 2,3- and 2,5-dihydroxybenzoic acids (with 2,3-dihydroxybenzoic acid being prominent) *versus* the estimated percentage of charge passed during the electrolysis. Error bars are the result of repeating the experiments in triplicate. As seen in Fig. 8, the highest product yield of *ca.* 21.6 ± 2.5% was obtained when 33.3% of charge (4.82 C) was consumed. After that the reaction yield was moderately decreased with further increasing electric charge passed as 2,3- and 2,5-dihydroxybenzoic acids were oxidised further to other reaction intermediates by more free •OH radical electrogenerated *in situ* as discussed earlier.[3,15,20,21] Typically, the number of electric charge passed during the electrolysis corresponded to the amount of H_2O_2 formed which then reacted with Fe(II), producing •OH radical. Thus, this simply implies that the greater the amount of charge passed, the greater the number of •OH radical electrogenerated. The complete (100%) conversion of salicylic acid to its monohydroxylated products (before further oxidation to other intermidiates) was not achieved as these primary monohydroxylated products which are more electron-rich aromatic compounds could be hydroxylated further by more free •OH radical electrogenerated *in situ*, resulting in the formation of polyhydroxylated products.

Note that the work reported here is a proof-of-concept study for the aromatic hydroxylation by hydroxyl radical electrogenerated by electro-Fenton reaction. Future research is planned to investigate the hydroxylation of aromatic drugs since the metabolites of aromatic drugs are often hydroxylated compounds.

4. Conclusions

The electrochemical behaviour of Fe(III) in the presence of either hydrogen peroxide (Fenton's reagent) or salicylic acid in 0.1 M Na_2SO_4 pH 3.0 has been investigated by cyclic voltammetry. The controlled-potential electrolysis was also conducted for the electrochemical generation of hydrogen peroxide *via* a two-proton-two-electron reduction of oxygen. The major advantage of hydrogen peroxide formed *in situ* within the electrochemical cell is that there is no need to store or transport the commercial one which is difficult to handle and requires chemical stabilisation. The actual concentration of hydrogen peroxide obtained from the electrolysis was then determined by the titration with potassium permanganate and

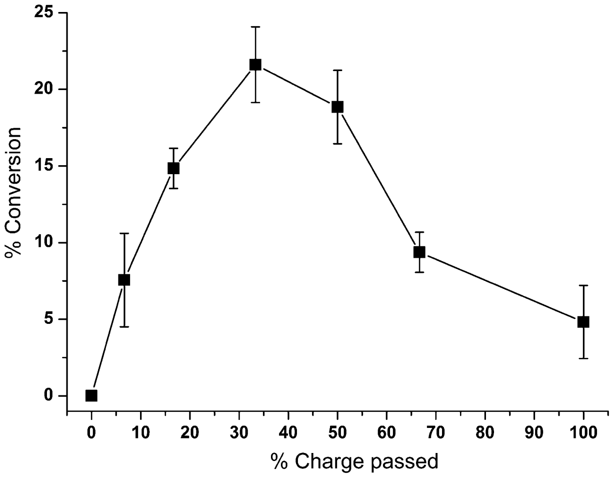


Fig. 8 Plot of % conversion of salicylic acid to its mono-hydroxylated derivatives *vs.* % charge passed during the electrolysis.

the electrolysis current efficiency for hydrogen peroxide electrogenerated was found to be *ca.* 85–97%. Furthermore, the preparative-scale hydroxylation of salicylic acid by hydroxyl radical electrogenerated from electro-Fenton process has been studied. An attack of hydroxyl radical on salicylic acid produced 2,3- and 2,5-dihydroxybenzoic acids with 2,3-dihydroxybenzoic acid as a major product. The highest yield of these two monohydroxylated products was found to be *ca.* 21.6 ± 2.5%. Despite the low product yield, this electrochemically assisted Fenton reaction appears to be a simple, fast and cheap method for preparing such hydroxylated derivatives in small amounts.

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