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Electrochemical oxidation of salicylhydroxamic acid on Pt electrode

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Abstract. The electrochemical oxidation behavior of salicylhydroxamic acid (SHAM) on a Pt electrode was investigated in aqueous solution of different pHs, containing 10 mM of SHAM, at 25 ◦C, by cyclic voltammetry technique. The results indicate that the SHAM was oxidized more easily in alkaline medium than acidic and neutral mediums, and the oxidation peaks of SHAM shifted toward lower potential values by increasing pH values. The SHAM electrooxidation involves an irreversible transfer of one or two electron, depending on the pH of solution. If solution pH is lower than 3 and higher than 7, the two electron transfer is involved in the electrooxidation. While, from pH=3 to pH=7, the SHAM electrooxidation involves an irreversible transfer of one electron and two protons in the first step, in agreement with the one step one-electron mechanism. The effect of SHAM concentration on the electrode reaction was investigated in artificial saliva solution. SHAM gives a single irreversible oxidation wave over the wide concentration range studied. Possible mechanism of SHAM electrooxidation was proposed.

Keywords: salicylhydroxamic acid, cyclic voltammetry, electrooxidation, platinum electrode.

1. Introduction

The systemic use of salicylic acid may cause severe irritations and it can be utilized only in external form. Thus, several derivatives have been synthesized. Hydroxamic acids refer to a class of organic compounds of the general formula RC(=O)N(R')OH, this type of acids being much weaker than the structurally related carboxylic acids [1].

The hydroxamic acids have a variety of applications in biology and medicine. These compounds possess antibacterial and antifungal properties and are selective inhibitors for a variety of enzymes such as peroxidases [2, 3], ureases [4], matrix metalloproteases [5, 6], hydrolases [7], and peptide deformylases [8]. This makes hydroxamic acids ideal candidates for drug design.

The salicylhydroxamic acid (SHAM) is a member of this family, known for its pharmaceutical applications. It prevents the formation of calcium oxalate stones in kidneys [9]. SHAM also prevents the formation of phosphate stones by inhibiting urease enzyme activity. The splitting of urea to ammonia and carbon dioxide is then catalyzed by the urease enzyme in cases of urinary tract infection. By inhibiting urease activity, SHAM reduces ammonia formation and retains urea acidic. It also reduces serum uric acid and reduces the incidence of ureate and uric stones [10].

Electrochemical oxidation of salicylic acid [11], salicylaldehyde [12] and acetylsalicylic acid [13] has been widely investigated focusing on the electrochemical removal and degradation, electrochemical detection [14], electro-polymerization [15] and electrooxidation mechanism [16]. Salicylic acid and its derivatives have also been used as electrode modifiers for the determination of trace Cu(II) in water [17], the amperometric nonenzymatic determination of glucose free of interference [18]. However, only a few reports are available on electrochemical oxidation of SHAM [19]. It is important to know the extent of hydrolysis of SHAM, because packing forms are important to consider since the drug degradation in the body depends on factors such as pH.

The aim of the investigations described in this paper was the determination of SHAM electrochemical behavior in the electrooxidation at platinum electrode, at different pH values and also in a solution which reproduced a physiological medium (*i.e.* artificial saliva).

2. Experimental

2.1. Materials

The salicylhydroxamic acid, SHAM, purchased from Sigma–Aldrich, was of analytical pure grade. Solutions used in the determination of pH effect on SHAM oxidation were prepared by dissolving the substrate in buffers. Phosphate buffer solutions with

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different pH values were prepared from stock solutions (0.1 M) of H_3PO_4, NaH_2PO_4, Na_2HPO_4, and NaOH. All reagents were of analytical grade. The artificial saliva composition was: NaCl 0.4 g/L; KCl 0.4 g/L; $CaCl_2$ 0.6004 g/L; $NaH_2PO_4 \cdot 2H_2O$ 0.78 g/L; KSCN 0.300 g/L; $Na_2S \cdot 9H_2O$ 0.005 g/L; urea 1.000 g/L. Solutions were prepared using doubly distilled water.

2.2. Measurement methods

The cyclic voltammetry, CV, was used in electrochemical measurements with a Voltalab PGZ 100 "*All-in-one*" potentiostat/galvanostat. The potentials were measured against and referred to the standard potential of the saturated calomel electrode, SCE (0.245 V *vs*. the standard hydrogen electrode, SHE). A three-electrode cell system including a saturated calomel electrode, as a reference electrode, a platinum wire as an auxiliary electrode, and the platinum geometric surface area of 0.5 cm^2, as the working electrode, were applied in the electrochemical studies. The pH of buffer solutions was measured using digital pH meter.

3. Results and Discussions

3.1 The effect of pH on SHAM electrooxidation

Voltammetric methods are frequently used for the characterization of electroactive systems. The electrode reactions of reduction and oxidation of SHAM at the platinum electrode were studied by cyclic voltammetry.

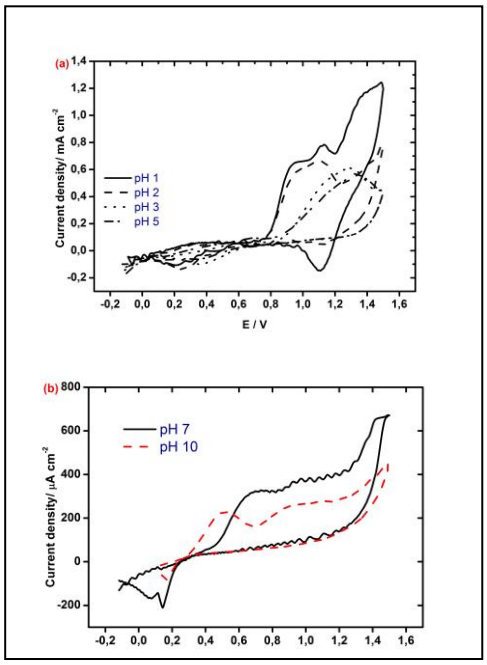


Figure 1. Cyclic voltammograms of SHAM in aqueous solution (pH = 1-10).

Cyclic voltammetric behavior of SHAM was examined in a wide pH range of 1–10 at 25 ˚C. The cyclic voltammograms shows different anodic peaks (Fig. 1), corresponding to the oxidation of SHAM.

The number and position of anodic peaks depend on the solution pH. The anodic peaks current density (i_p) first decreased with increasing pH, showing a minimum peak current at pH 10.0. Voltammograms presented in Fig. 1 ("a" and "b" curves) show that SHAM is oxidized probably reversibly at potentials lower than the potential at which oxygen evolution starts. Irreversibility of this electrode reaction needs to be proved. Three peaks visible in the cyclic voltammogram correspond to SHAM electrooxidation. This peaks have adsorptive character and corresponds to electrooxidation of a SHAM adsorbed form. At pH=3 and pH=5, only one peak was recorded, but in neutral and alkaline solution two peaks were measured.

The SHAM electrooxidation potential shifts towards more positive values with an increase in pH up to 5 then decreased again as show in Fig. 2.

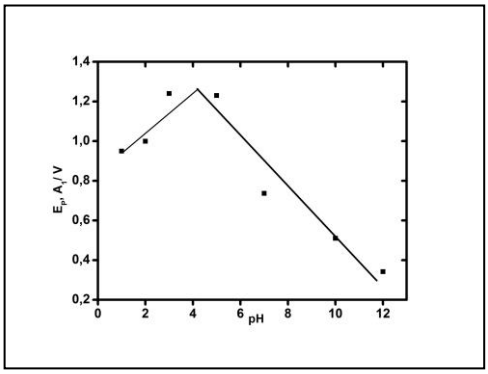


Figure 2. The pH dependence of the anodic peak potential.

3.2. Electrooxidation of SHAM in artificial saliva solution

The effect of SHAM concentration on the electrode reaction was investigated.

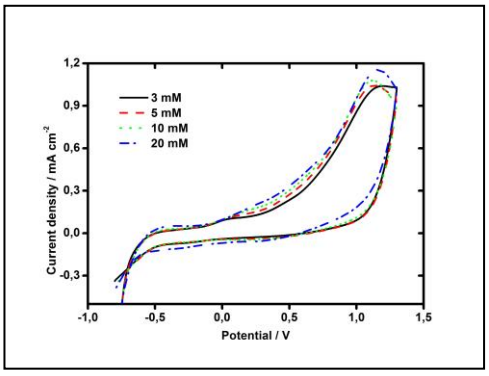


Figure 3. Cyclic voltammograms for different concentrations of SHAM oxidation at Pt electrode, recorded at 10 mV scan rates in artificial saliva solution.

Fig. 3 shows the cyclic voltammograms of SHAM at different concentrations (3, 5, 10 and 20 mM) in artificial saliva solution recorded at a scan rate of 10 mV·s^{-1}. When SHAM compound is added to the artificial saliva, the solution displays only one oxidation peak at potential range of 1.1 - 1.3 V (Fig. 3). The oxidation peak current density versus SHAM concentration is plotted and presented in Fig. 4. An increase in the concentration causes significant increase in the peak current.

Scan rate is one of parameters significantly affecting electrooxidation of compounds. Thus, an effect of the scan rate on SHAM electrooxidation was investigated in the range from 0.01 to 0.2 V·s^{-1} using cyclic voltammetry methods (Fig. 4).

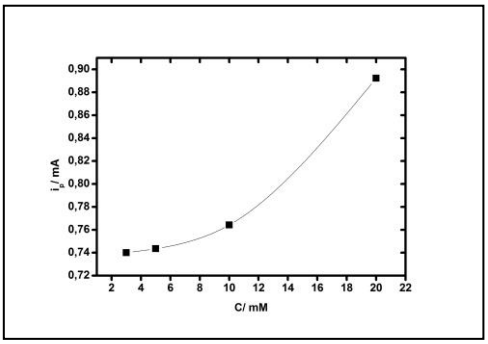


Figure 4. Dependence of the anodic peak current on SHAM concentration.

Cyclic voltammograms were used in determination of peak current and potential for the SHAM electrooxidation. Two approaches widely used to study the reversibility of reactions and to determine whether a reaction is adsorption or diffusion controlled consist of the analyses of dependences: i_p on $v^{1/2}$.

Fig. 5 shows these plots for the oxidation peak of SHAM in artificial saliva solution at 25 °C. For reversible or irreversible systems without kinetic complications, i_p varies linearly with $v^{1/2}$, intercepting the origin. Although, the plot of i_p on $v^{1/2}$ presented in Fig. 6a is linear, it does not cross the origin of the axes. This is characteristic for the electrode process preceded or followed by a homogenous chemical reaction. In the scan rate range from 0.01 to 0.2 V·s^{-1}, peak current (i_p) of SHAM electrooxidation depends linearly on square root of the scan rate (v) and is described by the following equation:

$$i_p = \{0.5949\ [v\ (\mathrm{V\ s^{-1}})]^{1/2}\}\ \mathrm{mA} + 0.53117\ \mathrm{mA}$$

This dependence does not cross the origin. This fact can suggest that the electrode process of SHAM electrooxidation is controlled by diffusion and can be preceded by chemical reaction.

Fig. 6b presents a dependence of E_p on scan rate determined from cyclic voltammograms recorded for the SHAM electrooxidation. If electrochemical reaction is reversible, then E_p is independent on v. Thus, it can be concluded that heterogeneous electron transfer in SHAM electrooxidation is irreversible because E_p increases with an increase in the scan rate.

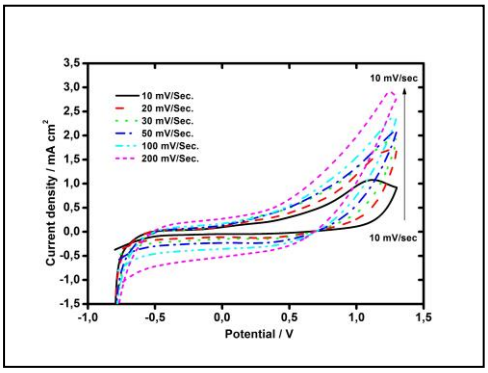
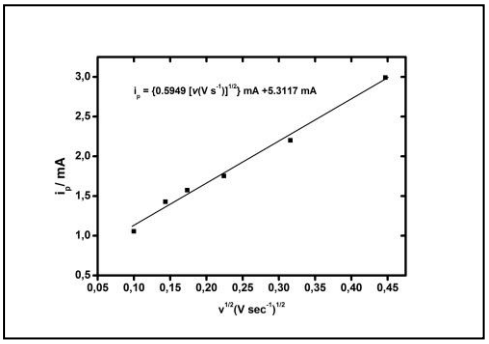


Figure 5. Cyclic voltammograms of SHAM oxidation at Pt electrode, recorded at various scan rates in artificial saliva solution.

(a)



(b)

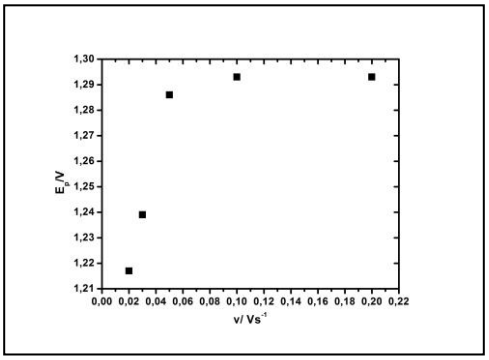
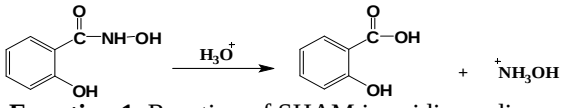
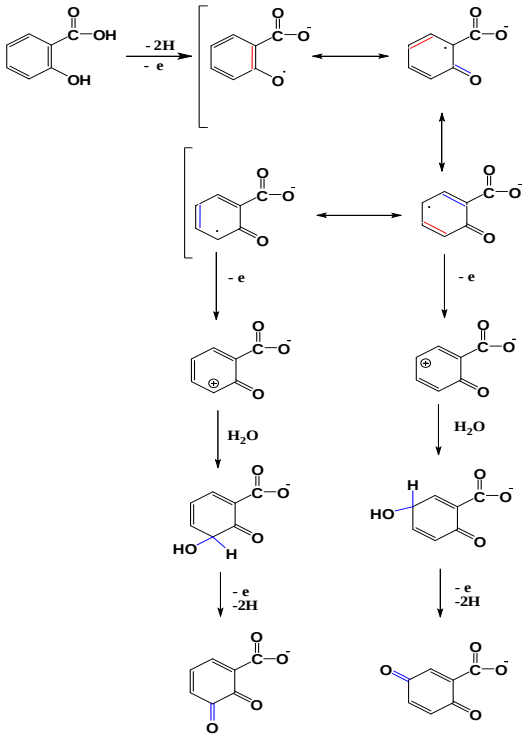


Figure 6. (a) Dependence of anodic peak current on the potential scan rate for the oxidation of SHAM at Pt electrode (c = 10 mM in artificial saliva solution). (b) Dependence of peak potential (E_p) on the potential scan rate (v) for the oxidation of SHAM in artificial saliva solution at Pt electrode.



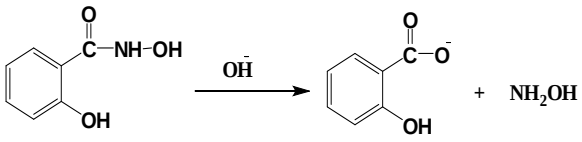
Equation 1. Reaction of SHAM in acidic medium.

We proposed consecutive reaction mechanism for electrochemical oxidation of SHAM in acidic medium. SHAM was converted to salicylic acid as in Eq. 1. Initially, the phenoxy carboxylate radical was formed through one electron and two-proton oxidation. The phenoxy carboxylate radical underwent tautomerism and oxidation, forming 2-oxocyclohexa-3,5-dien-1-ylium carboxylate and 4-oxocyclohexa-2,5-dien-1-ylium carboxylate, which hydrolyzed to obtained 5-hydroxy-6-oxocyclohexa-1,3-dienecarboxylate and 3-hydroxy-6-oxocyclohexa-1,4-dienecarboxylate respectively, followed by the third oxidation by loss of one electron and two protons to form 5,6-dioxocyclohexa-1,3-dienecarboxylate and 3,6-dioxocyclohexa-1,4-dienecarboxylate (Scheme 1) [19-22].



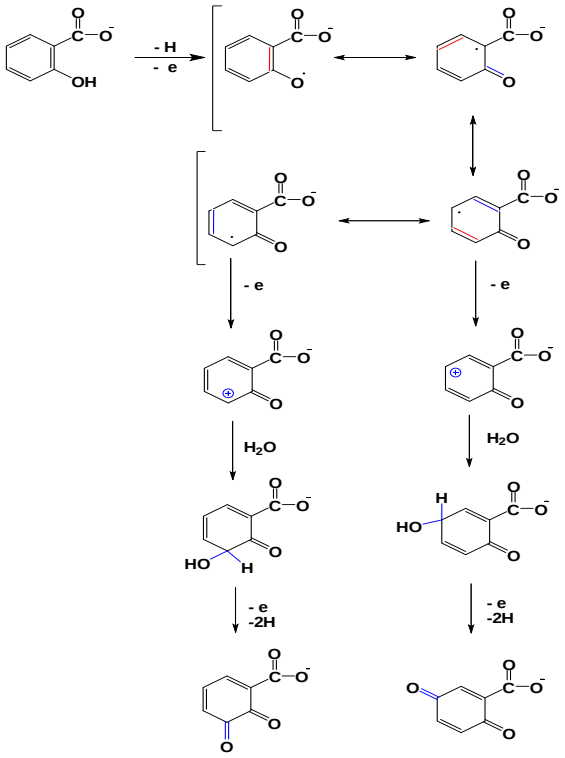
Scheme 1. The oxidation of salicylic acid in acidic medium.

In basic medium, SHAM was converted to *o*-hydroxybenzoate ion (salicylate ion) as shown in Eq. 2**.**



Equation 2. Reaction of SHAM in basic medium.

Oxidation of salicylate ion through one electron and one proton gave phenoxy carboxylate radical, which underwent tautomerism and oxidation form 2-oxocyclohexa-3,5-dien-1-yliumcarboxylate and 4-oxocyclohexa-2,5-dien-1-yliumcarboxylate and so on as mentioned before in acidic medium (Scheme 2).



Scheme 2. The oxidation of salicylic acid in basic medium.

4. Conclusions

The electrooxidation behavior of salicylhydroxamic acid was investigated at Pt electrode. The SHAM is electrochemically oxidized in at least two electrode steps. The electrode reactions are preceded by SHAM hydrolysis, resulting in the formation of the salicylic acid and ammonia, which further undergo electrooxidation. The mechanism of SHAM electrooxidation depends on pH of reaction medium. The peak at cyclic voltammograms corresponds to SHAM oxidation reaction which is diffusion controlled. The increase in pH above 3, causes the change in SHAM oxidation mechanism.

The electrochemical oxidation of SHAM on Pt electrode was performed in artificial saliva solution at various substrate concentrations and scan rate. The SHAM electrochemical oxidation is an irreversible reaction at a platinum electrode. The peak at cyclic voltammograms corresponds to SHAM oxidation reaction which is diffusion controlled.

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