




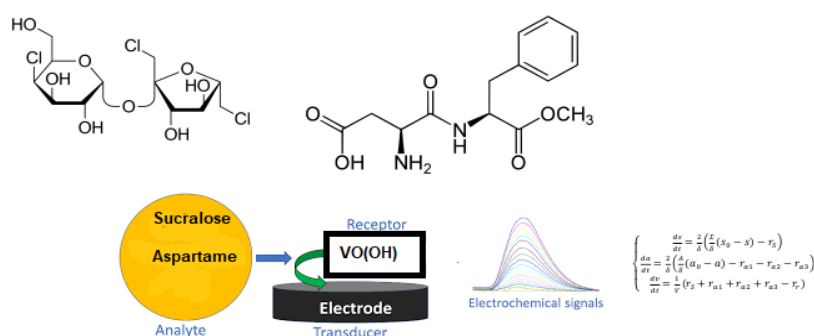
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The Theoretical Description for the Electrochemical Determination of Sucralose and Aspartame in Drinks

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In this work, the electrochemical determination of sucralose and aspartame in drinks has been theoretically evaluated. Considering the accepting character of both sucralose chlorine atom and aspartame molecule, cathodic process is preferred. The theoretical description for VO(OH)-assisted electroanalytical process has proven the efficiency of the cathodic electroanalytical process for both of the sweeteners, despite of the augmented probability of the oscillatory behavior.

Graphical abstract



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1. Introduction

Sucralose (Fig. 1) is one of the most used sweeteners in Portugal and throughout the European Union in the alimentary and pharmaceutical industries, as a flavor corrector. [1 - 5]. In the USA it is also known by its registered trademark Splenda®. In Codex Alimentarius it is registered as E955. It is a trichlorosubstituted derivative of galactosucrose, which has twice the sweetness of saccharin, triple the sweetness of aspartame and is up to a thousand times as sweet as the common sugar. When it comes to physical properties, free sucralose is a white, shiny, odorless substance, soluble in water.

Although sucralose is a derivative of natural compounds, it itself is not a natural compound. They synthesize it from

sucrose, in several steps (Fig. 2).

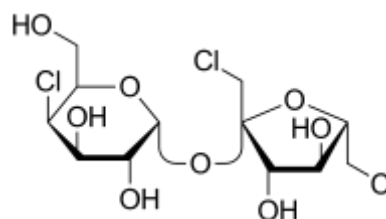


Fig. 1. Sucralose.

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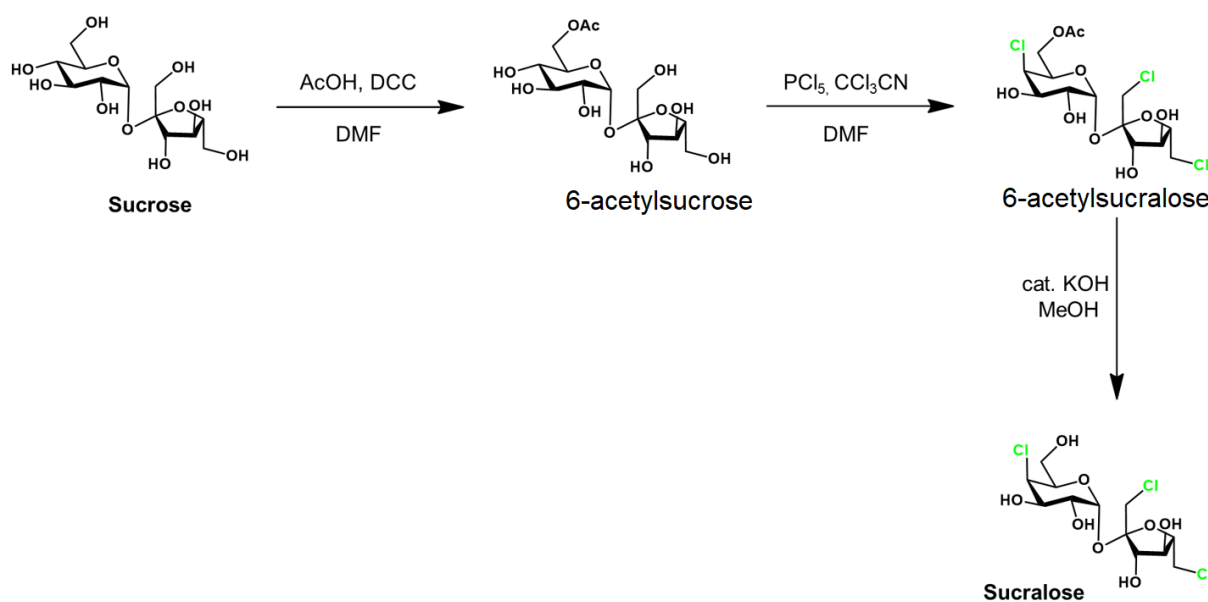


Fig. 2. Sucralose synthesis from sucrose.

The acylation on the first stage may also be made by diethylazodicarboxylate. The C4 epimerization (mutarotation) is realized on the second stage. This synthesis involves either the toxic reagents (DCC, DAAD and PCl_5) or intermediate (6-acetylsucralose) as mentioned below.

Despite of being considered safe for use by diabetics and athletes, its harmful effects on human health and the environment are still unknown, and some of its negative effects have only begun to be studied now. A recent study involving pregnant and breastfeeding women [6 – 8] confirms that sucralose enters breast milk, causing irreparable damage to the development of the gut microbiota of the human fetus in the last months of pregnancy, as well as in neonates and babies, reason why its safety for use during pregnancy and breastfeeding is still questioned.

Moreover, as sucralose is nearly not biodegradable, it is accumulated in the environment [9-10]. Furthermore, when sucralose decomposes thermally or by some bacteria, it transforms into toxic compounds such as dioxins and tetrachlorodibenzofurans. It should not be forgotten that sucralose is also part of the group of halogenorganic compounds (Fig. 3). Therefore, the development of a method for sucralose determination in beverages and the environment is truly current [11 – 12].

On the other hand, aspartame [13 – 15] (Fig. 3) is a sweetener firstly developed in 1965 by Monsanto and registered in Codex Alimentarius as E951. It is the sweetener, mostly used in drinks and beverages, inclusively alongside with sucralose. It is formed from phenylalanine methyl ester and aspartic acid.

Nevertheless, its intake may be associated with diabetes mellitus aggravation, methanol intoxication, pathogenesis of some mental deficiencies [16 – 20]. Moreover, some recent investigations indicate the possible carcinogenesis of aspartame. For this reason, the determination of aspartame is really up to date [21 – 23], and the electroanalytical methods, yet used for the similar compounds [24 – 30], could be applied also to aspartame and sucralose simultaneous determination.

Considering the chemical composition of both sucralose and aspartame, we consider that both cathodic and anodic

processes are viable. Nevertheless, as aspartame is highly accepting molecule, the cathodic process is more preferable. Moreover, it is realized in mildly acidic pH, correspondent to most of the soft and alcoholic drinks.

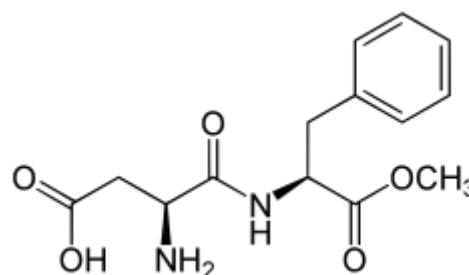


Fig. 3. Aspartame.

On the other hand, the development of new electrosynthesis, electroanalysis and electrochemical conversion processes requires *a priori* theoretical investigation of the system's behavior. This investigation allows you to solve problems such as:

- the uncertainty surrounding some details of the electroanalytical process (how electroreduction is carried out under specific conditions, what modifiers could be used there);

- the possibility of the appearance of instabilities, characteristic for the electrooxidation of organic compounds, including electropolymerization [31 – 32].

Therefore, the general objective of this work is to evaluate the performance of the electrochemical detection of sucralose and aspartame through a cathodic process, assisted by conducting polymer containing the basic groups (organic amine and/or pyridinic nitrogen atoms). Furthermore, the behavior of this system will be compared with that of similar systems [33 – 35].

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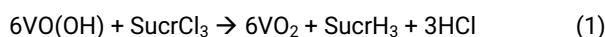
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2. Material and Methods

2.1 System and its modeling

The electrochemical reduction of sucralose on VO(OH)-modified electrode will be carried out by chlorine atoms and will follow the reaction (1):



Desoxygalactosucrose is a product of this reaction, reason why it is used for sucralose removal from the environment. As for the aspartame, it will be reduced via esterified and non-esterified carboxyl and via ketogroup.

Taking this into account, we describe the behavior of this system by a trivariant equation-set (2):

$$\begin{cases} \frac{ds}{dt} = \frac{2}{\delta} \left(\frac{\Sigma}{\delta} (s_0 - s) - r_s \right) \\ \frac{da}{dt} = \frac{2}{\delta} \left(\frac{A}{\delta} (a_0 - a) - r_{a1} - r_{a2} - r_{a3} \right) \\ \frac{dv}{dt} = \frac{1}{V} (r_s + r_{a1} + r_{a2} + r_{a3} - r_r) \end{cases} \quad (2)$$

Herein a and s are aspartame and sucralose pre-surface concentrations, a_0 and s_0 are their correspondent bulk concentrations Σ and A stand for diffusion coefficients, δ is the pre-surface layer thickness, v is vanadium dioxide surface coverage degree, V is its maximal concentration, and the parameters r are the correspondent reaction rates, calculated as (3 - 7):

$$r_s = k_s s (1 - v)^6 \exp(-\alpha s) \quad (3)$$

$$r_{a1} = k_{a1} a (1 - v)^8 \quad (4)$$

$$r_{a2} = k_{a2} a (1 - v)^6 \quad (5)$$

$$r_{a3} = k_{a3} a (1 - v)^4 \quad (6)$$

$$r_r = k_r v \exp\left(-\frac{F\phi_0}{RT}\right) \quad (7)$$

Herein the parameters k stand for the correspondent reactions rate constants, α is the parameter, relating DEL electrochemical and electrophysical properties to ionic forms interchange during the chemical immobilization, $F = N_A \cdot e$ is the Faraday number, ϕ_0 is zero-charge related potential slope, R is the universal gas constant and T is the absolute reaction temperature.

Considering the formation of chloride-ion during the

chemical stage, the oscillatory behavior probability enhances in relation to the simplest case. Nevertheless, this augmentation won't influence much the electroanalytical efficacy of the system, as shown below.

3. Results and Discussion

In order to investigate the behavior of the VO(OH)-assisted sucralose and aspartame electrochemical determination, we analyze the equation-set (2), alongside with the algebraic relations (3 - 7) by means of linear stability theory. The steady-state Jacobian functional matrix members may be exposed as:

$$\begin{pmatrix} a_{11} & a_{12} & a_{13} \\ a_{21} & a_{22} & a_{23} \\ a_{31} & a_{32} & a_{33} \end{pmatrix} \quad (8)$$

In which:

$$a_{11} = \frac{2}{\delta} \left(-\frac{\Sigma}{\delta} - k_s (1 - v)^6 \exp(-\alpha s) + \alpha k_s s (1 - v)^6 \exp(-\alpha s) \right) \quad (9)$$

$$a_{12} = 0 \quad (10)$$

$$a_{13} = \frac{2}{\delta} (6k_s s (1 - v)^5 \exp(-\alpha s)) \quad (11)$$

$$a_{21} = 0 \quad (12)$$

$$a_{22} = \frac{2}{\delta} \left(-\frac{A}{\delta} - k_{a1} (1 - v)^8 - k_{a2} (1 - v)^6 - k_{a3} (1 - v)^4 \right) \quad (13)$$

$$a_{23} = \frac{2}{\delta} (8k_{a1} a (1 - v)^7 + 6k_{a2} a (1 - v)^5 + k_{a3} a (1 - v)^4) \quad (14)$$

$$a_{31} = \frac{1}{V} (k_s (1 - v)^6 \exp(-\alpha s) - \alpha k_s s (1 - v)^6 \exp(-\alpha s)) \quad (15)$$

$$a_{32} = \frac{1}{V} (k_{a1} (1 - v)^8 + k_{a2} (1 - v)^6 + k_{a3} (1 - v)^4) \quad (16)$$

$$a_{33} = \frac{1}{V} \left(-6k_s s (1 - v)^5 \exp(-\alpha s) - 8k_{a1} a (1 - v)^7 - 6k_{a2} a (1 - v)^5 - k_{a3} a (1 - v)^4 - k_r \exp\left(-\frac{F\phi_0}{RT}\right) + jk_r v \exp\left(-\frac{F\phi_0}{RT}\right) \right) \quad (17)$$

Avoiding the cumbersome expressions during the determinant analysis, we rewrite the Jacobian determinant as (18):

$$\frac{4}{\delta^2 P} \begin{vmatrix} -\kappa - \Xi & 0 & T \\ 0 & -\xi - \Sigma & \Phi \\ \Xi & \Sigma & -T - \Phi - \Omega \end{vmatrix} \quad (18)$$

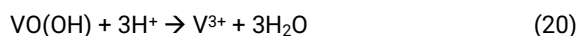
Opening the straight brackets, applying both Routh-Hurwitz stability criterion and monotonic instability condition and changing the signs to the opposite, we obtain the requirement set, expressed as (19):

$$\begin{cases} \kappa(\xi T + \xi \Phi + \xi \Omega + \Sigma T + \Sigma \Omega) + \Xi(\xi \Phi + \xi \Omega + \Sigma \Omega) > 0, & \text{linear dependence} \\ \Xi \Omega = 0, & \text{detection limit} \end{cases} \quad (19)$$

If $-\text{Det } J > 0$, the Routh-Hurwitz stability criterion is valid, and the steady-state is thereby stable, providing an efficient steady-state determination of both of the sweeteners. Moreover, the wide stability region lets use this system in pharmaceutical formulations and biological liquids, like also in the beverages.

This criterion is readily satisfied, if the kinetic parameters Σ , and Ω are positive. In the vast majority of the cases, they

both have positive signs and, considering that the other variables in the determinant are positive, it indicates the vast steady-state stability topological region. The electroanalytical process is mostly kinetically controlled, but with the possibility to transition to diffusion-controlled mode if $\text{pH} \rightarrow 0$. Nevertheless, considering the reaction:



The working pH will be limited to $\text{pH}=3$.

In the absence of the side reactions or other factors, capable to compromise the analyte and (or) modifier stability, excluding the reactions, foreseen by the mechanism, the linearity between the electrochemical parameter and concentration is observed, providing an efficient analytical signal interpretation, which is really important for drug concentration monitoring.

The condition $\text{Det } J=0$ corresponds to the detection limit, manifested by the *monotonic instability*. It may be seen as an N-shaped part of the steady-state voltammogram and depicts the margin between the stable steady-states and unstable states and corresponds to the steady-state multiplicity. In other words, multiple steady-states, each one unstable, coexist in this point.

As for the oscillatory behavior, it is realized beyond the detection limit, in the case of the Hopf bifurcation realization. Its realization requires the presence of the positive-callback related positive addendums in main diagonal elements.

Observing the main diagonal elements (9), (13) and (17), we may observe that the oscillatory behavior becomes possible, if the kinetic parameters α and j are positive, which corresponds to the DEL influences of all the chemical and electrochemical stages. This factor is typical for the similar systems [31 – 35] and may be described by the positivity of the element $\alpha k_{ss}(1 - v)^6 \exp(-\alpha s) > 0$ if $\alpha > 0$, describing ionic forms cyclic transformations during the sucralose reduction, and $j k_{rv} \exp\left(-\frac{F\phi_0}{RT}\right) > 0$, if $j > 0$, describing the similar cyclic phenomena on both DEL and surface during the electrochemical stages. These elements describe the positive callback, and this callback will depend on the system's characteristics. For example, the oscillation frequency and amplitude will depend on the background electrolyte composition, which has been proven experimentally and theoretically [31 – 35].

The same equation-set also describes the simultaneous cathodic electrochemical determination of sucralose with neotame, acesulfame K and saccharine (E952 – E954), as their cathodic behavior will become similar.

4. Conclusions

From the analysis of the process with the cathodic detection of sucralose and aspartame, assisted by vanadium oxyhydroxide, it is possible to conclude that in the present process, the steady-state is easy to obtain and maintain, providing an efficient analytical signal interpretation. The electrochemical process is mostly kinetically controlled, passing to diffusion-controlled mode at low pH. Nevertheless, the working pH is limited to $\text{pH}=3$. The oscillatory behavior is possible in this system. It is caused by periodic effects on the structure of the double electric layer. These effects are observed at both chemical and electrochemical stage.

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Author Contributions

Volodymyr V. Tkach (Investigation, Conceptualization, Supervision, Validation, Writing – Original Draft, Writing – Review and Editing); Tetiana V. Morozova (Conceptualization, Investigation, Supervision, Formal Analysis); Nataliia P. Shapovalova (Conceptualization, Investigation, Supervision, Formal Analysis).

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