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Electrochemical detection of doxorubicin and simvastatin for their combined use in the treatment of cancer

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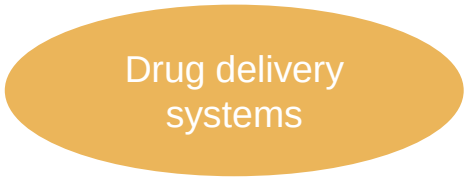
Introduction

- **Doxorubicin:**
  - Anti-tumor drug widely used;
  - Found on the market in different pharmaceutical forms;
  - Efficient;
  - Causes important side effects.

- **Simvastatin:**
  - Inhibitor of HMG-CoA reductase;
  - Used in the treatment of hypercholesterolemia;
  - In high doses decreases cell proliferation and potentiates the activity of anti-tumor drugs.



Outline of the study

01 Electrochemical characterization of doxorubicin

02 Electrochemical characterization of simvastatin

03 Simultaneous detection of doxorubicin and simvastatin

- Linear Sweep Voltammetry
- Chronoamperometry

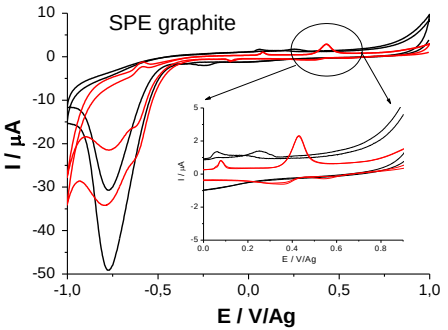
01. Electrochemical characterization of doxorubicin

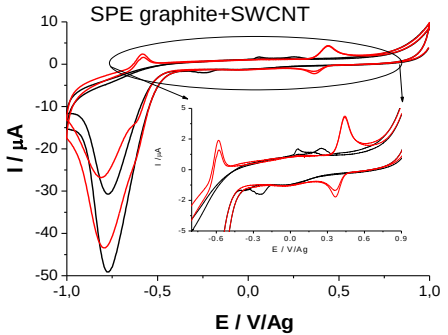
- Influence of the electrode material;
- Influence of the electrolyte and pH;
- Influence of the scan rate.

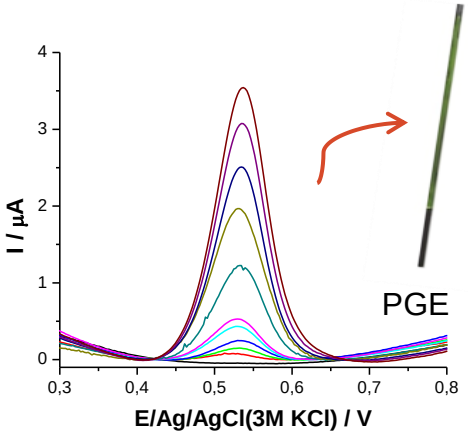
Electrochemical characterization of doxorubicin

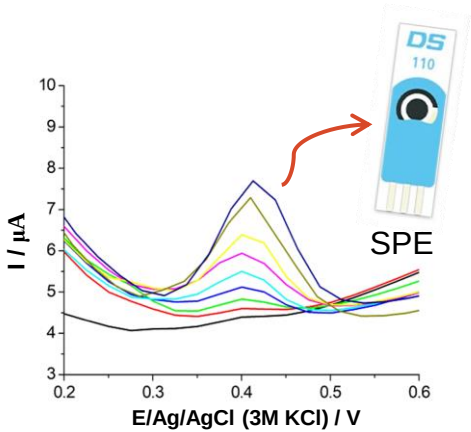
- Different types of electrodes were tested:
  - Graphite based SPE;
  - Gold based SPE;
  - Platinum based SPE;
  - Pencil graphite electrode (PGE);

Best results









Electrochemical characterization of doxorubicin

- The influence of the electrolyte and pH of the solution

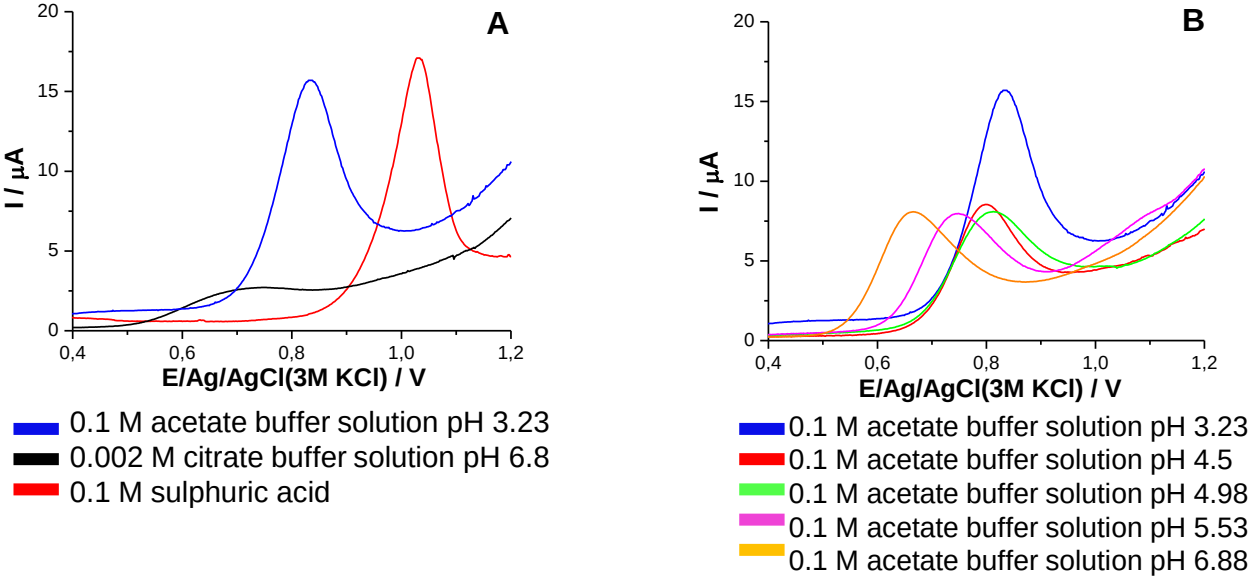


Figure A. DPVs of 10 µg/mL Dox in different electrolyte solutions
Figure B. DPVs of 10 µg/mL Dox in acetate buffer of different pH

Electrochemical characterization of doxorubicin

- The influence of the scan rate

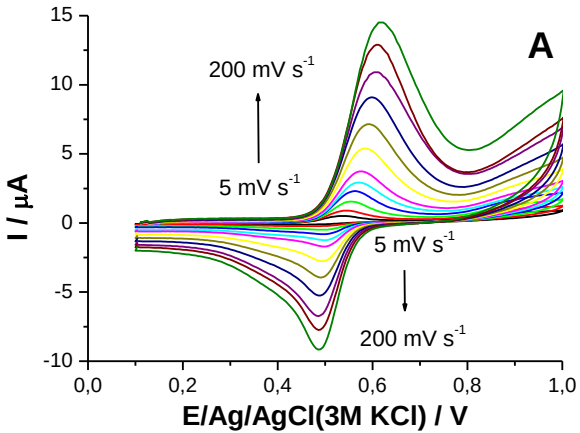


Table 1. Variation of the analytical current of Dox with the scan rate and square root of the scan rate

$I_{Ox} = 0.01\ v + 0.43$	$R^2 = 0.989$
$I_{Ox} = 0.20\ v^{1/2} - 0.12$	$R^2 = 0.988$
$I_{Red} = -0.01\ v - 0.09$	$R^2 = 0.996$
$I_{Red} = -0.15\ v^{1/2} + 0.33$	$R^2 = 0.983$

Figure A. CVs of 10 µg/mL Dox solution using PGE and different scan rates

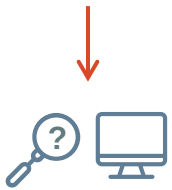
02. Electrochemical characterization of simvastatin

- Influence of the electrode material;
- Influence of the pH;
- Influence of the scan rate.

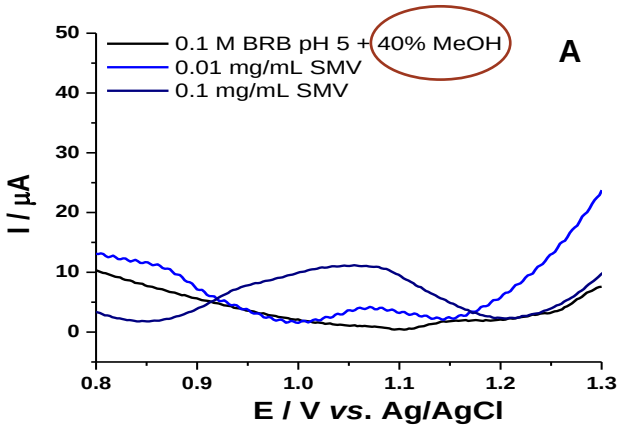
Electrochemical characterization of simvastatin

- The influence of the electrode material

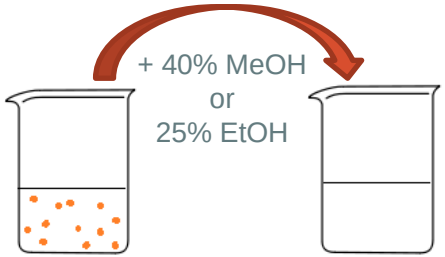
PGE



Graphite based SPE



Dissolution of SMV



SMV aqueous solution

Figure A. The analytical signal of SMV in LSV, on graphite SPE

Electrochemical characterization of simvastatin

- The influence of the pH

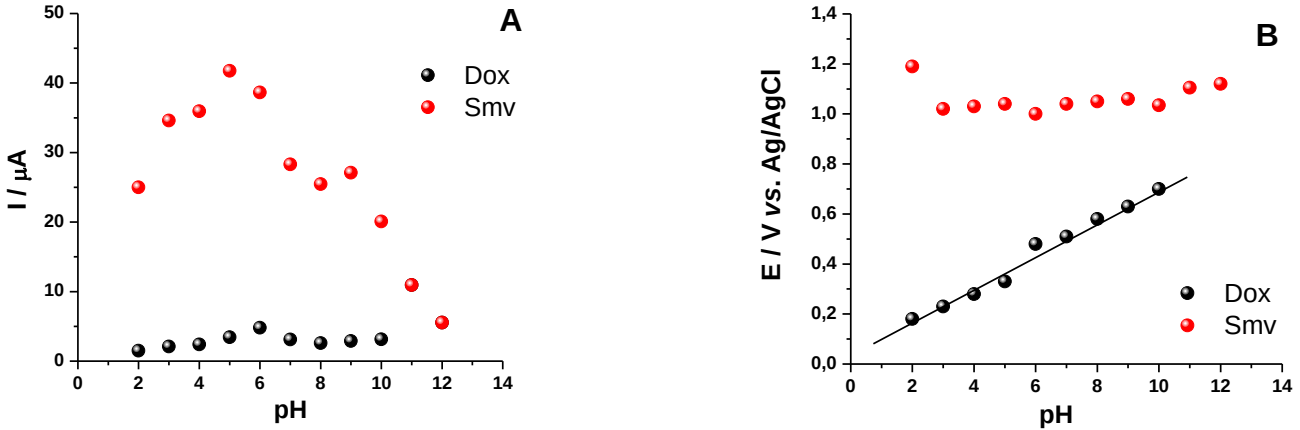


Figure A. Variation of the analytical signal of Smv with pH, compared to Dox
Figure B. Variation of the oxidation potential of Smv with pH, compared to Dox

Electrochemical characterization of simvastatin

- The influence of scan rate

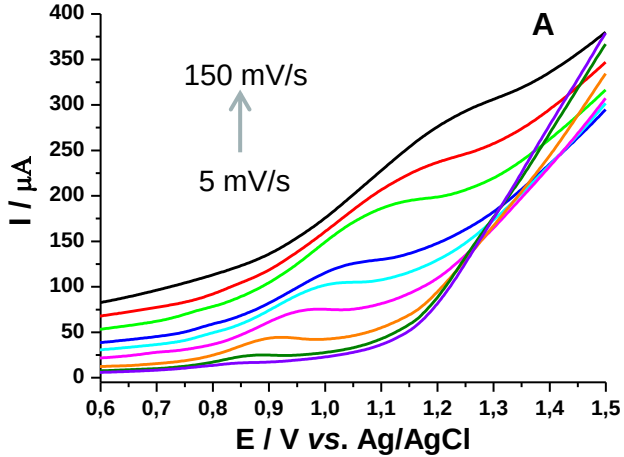


Table 1. Variation of the analytical current of Smv with the scan rate and square root of the scan rate

I_{Ox} = 0.1547 v + 2.2451	R^2 = 0.9666
I_{Ox} = 2.2753 $v^{1/2}$ – 4.2989	R^2 = 0.9847

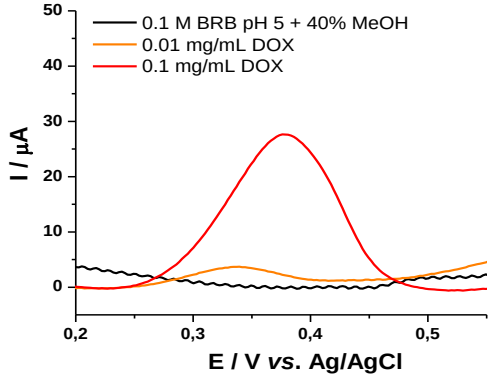
Figure A. Variation of the analytical signal of 0.1 mg/ml Smv with the scan rate: 250 mV/s (black), 200 mV/s (red), 150 mV/s (green), 100 mV/s (blue), 75 mV/s (cyan), 50 mV/s (magenta), 25 mV/s (orange), 10 mV/s (dark green), 5 mV/s (violet)

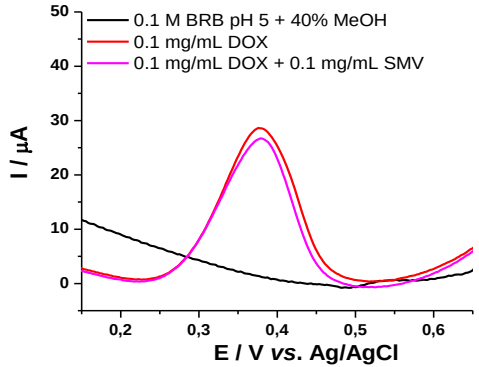
03. Simultaneous detection of doxorubicin and simvastatin

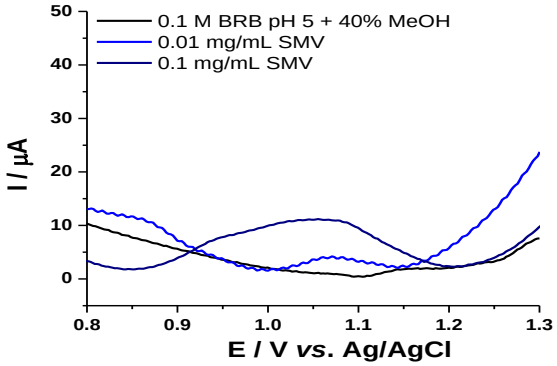
- Linear Sweep Voltammetry
- Chronoamperometry

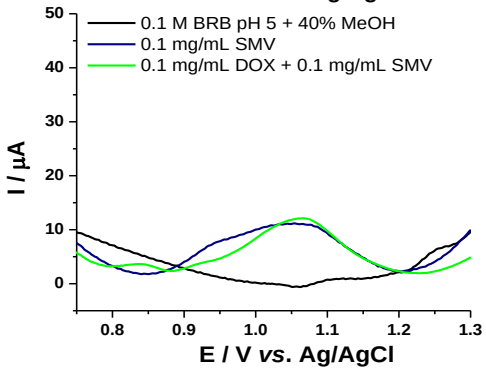
Simultaneous detection of doxorubicin and simvastatin

- Linear Sweep Voltammetry









Simultaneous detection of doxorubicin and simvastatin

- Chronoamperometry

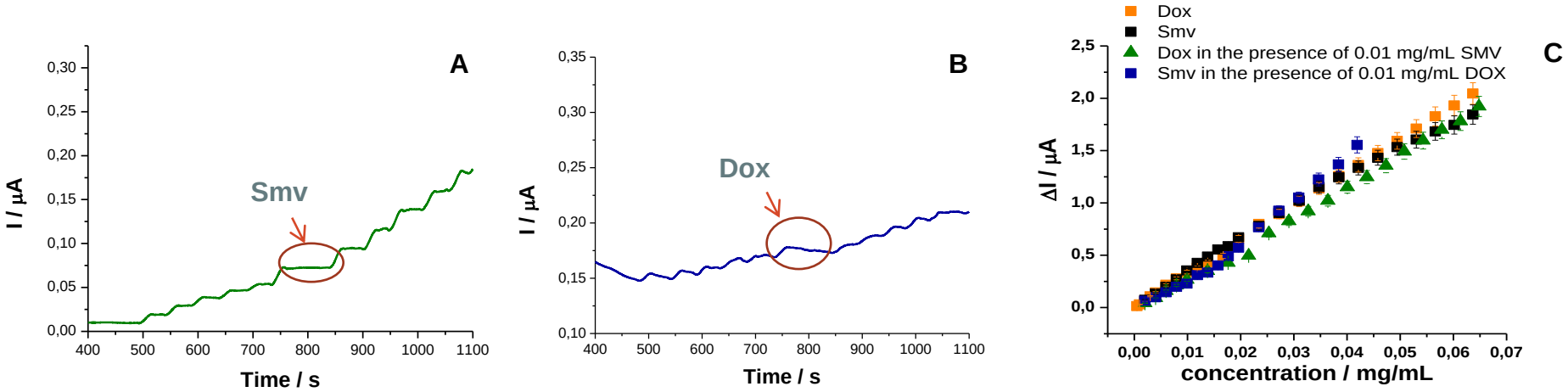


Figure A. Addition of Smv between succesive additions of Dox in PB pH 5+25% EtOH, in chronoamperometry at 0.5 V.
Figure B. Addition of Dox between succesive additions of Smv in PB pH 5+25% EtOH, in chronoamperometry at 0.95 V.
Figure C. Variation of the analytical current of Dox alone, Dox in the presence of Smv, Smv alone and Smv in the presence of Dox.

Simultaneous detection of doxorubicin and simvastatin

Analyte	LSV	Amperometry
Dox	I (μA) = 273.3 [Dox] (mg/mL) + 1.18 R^2=0.997; Range: 0.001 – 0.1 mg/mL	I (μA) = 32.1 [Dox] (mg/mL) + 0.009 R^2=0.999; Range: 0.0005 – 0.065 mg/mL
Dox + 0.01 mg/mL Smv	I (μA) = 311.4 [Dox] (mg/mL) + 0.72 R^2=0.968; Range: 0.001 – 0.01 mg/mL	I (μA) = 29.97 [Dox] (mg/mL) - 0.049 R^2=0.997; Range: 0.002 – 0.065 mg/mL
Smv	I (μA) = 100.1 [Smv] (mg/mL) + 0.40 R^2=0.996; Range: 0.005 – 0.5 mg/mL	I (μA) = 29.04 [Smv] (mg/mL) + 0.073 R^2=0.994; Range: 0.002 – 0.065 mg/mL
Smv + 0.01 mg/mL Dox	I (μA) = 73.62 [Smv] (mg/mL) + 0.70 R^2=0.914; Range: 0.02 – 0.1 mg/mL	I (μA) = 38.16 [Smv] (mg/mL) - 0.12 R^2=0.987; Range: 0.002 – 0.45 mg/mL

Applications

Analysis of different pharmaceutical forms containing Dox or Smv

Control of encapsulation and release of Dox and Smv from drug delivery systems containing both substances

Conclusions

- The electrochemical behaviors of doxorubicin and simvastatin were studied;
- Two analytical strategies were successfully developed for the simultaneous detection of these molecules;
- Chronoamperometry proved to have a better sensitivity for the analysis of simvastatin;
- This detection strategy represents a promising tool in the development of new pharmaceutical forms or drug delivery systems containing both drugs whose association was proved to bring benefits in the treatment of cancer.

Thank you for your attention!

Achnowledgements:
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