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Highly sensitive voltammetric sensors based on selenium dioxide nanoparticles for the quantification of colorants in pharmaceutical dosage forms

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pharmaceuticals MDPI

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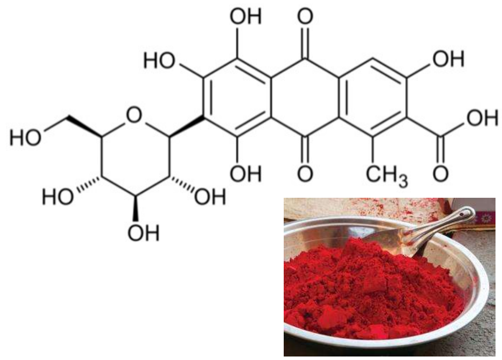
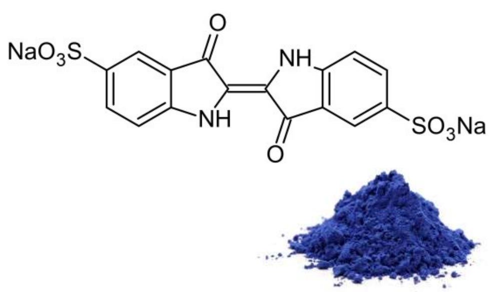
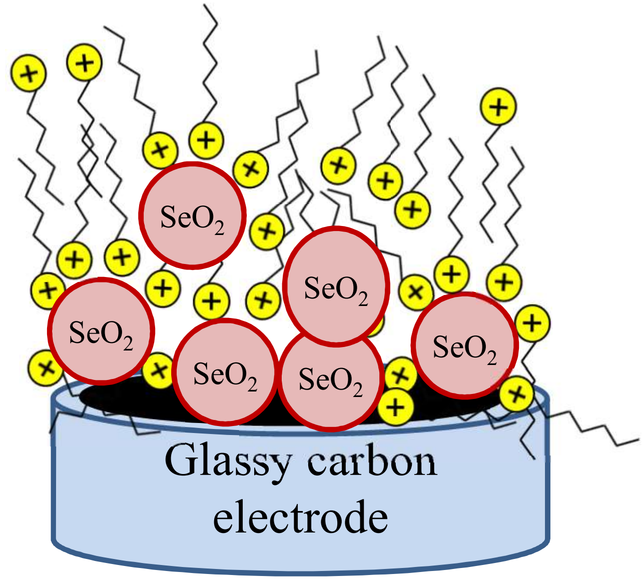
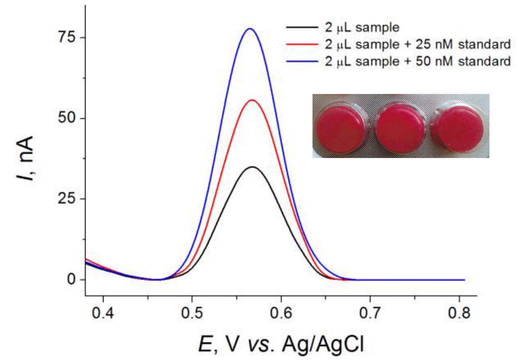
Carminic acid

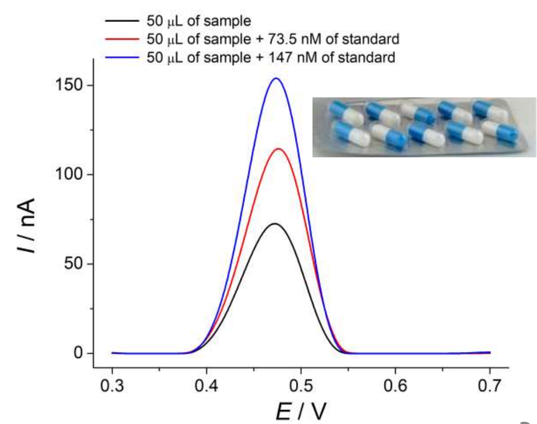


Indigotine









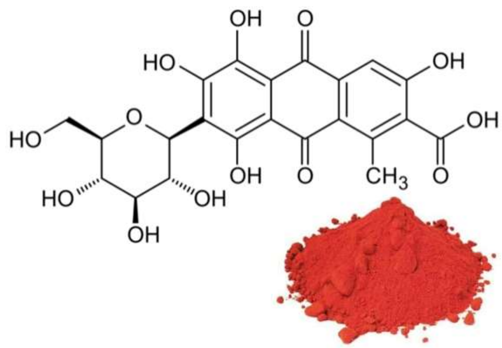
Abstract:
Colorants, in particular, carminic acid and indigotine are widely used in pharmaceutical industry. High concentration of these colorants affect human health that require a control of their content in pharmaceutical dosage forms. In current work, novel voltametric sensors based on glassy carbon electrodes modified with selenium dioxide nanoparticles dispersed in surfactant media have been developed for the determination of carminic acid and indigotine. Combination of selenium dioxide nanoparticles with surfactant media provides stabilization of nanoparticles dispersion by suppression of their aggregation as well as action of the surfactant as a co-modifier of the electrode surface, i.e. as a part of sensing layer of the electrode. The effect of surfactant nature (cationic, nonionic, and anionic) and concentration on the colorants' voltammetric characteristics has been investigated. The best response of colorants has been obtained in the case of selenium dioxide nanoparticles dispersed in cationic surfactants (0.10 mM cetyltriphenylphosphonium bromide for carminic acid and 1.0 mM cetylpyridinium bromide for indigotine). The sensors developed have been used under conditions of differential pulse voltammetry in acidic medium. A linear dynamic ranges of 0.010–2.5 and 2.5–10 μM of carminic acid and 0.025–1.0 and 1.0–10 μM of indigotine with the detection limits of 3.4 and 4.3 nM, respectively, have been achieved that are the best ones among the methods reported to date. Another advantage of the sensors developed is a simple one-step fabrication as well as easy and fast preparation of the modifier. Sensors have been successfully applied in the analysis of pharmaceutical dosage forms (vitamin tablets, capsules, and lozenges for sore throat treatment) and validated with spectrophotometry. The direct analysis of colorants in various pharmaceutical dosage forms confirms versatility of the sensors developed that can be used as an alternative method for the quality control of the pharmaceutical products.

Keywords: voltammetric sensors; modified electrodes; selenium dioxide nanoparticles; surfactants; colorants; carminic acid; indigotine; pharmaceutical analysis

Introduction

Colorants in pharmaceutical industry

Carminic acid (E120)



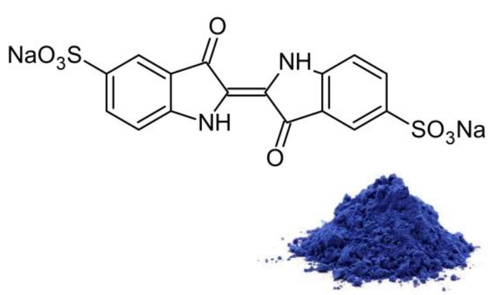
The acceptable daily intake is

2.5 mg/kg bw/day

Negative health effects

- allergic reactions of various severity including anaphylactic reaction

Indigotine (E132)



5.0 mg/kg bw/day

- side effects in the liver, central nervous system, kidneys, and eyes
- mutagenic effects leading to oncogenesis

Control of colorants in pharmaceutical dosage forms is required

Introduction

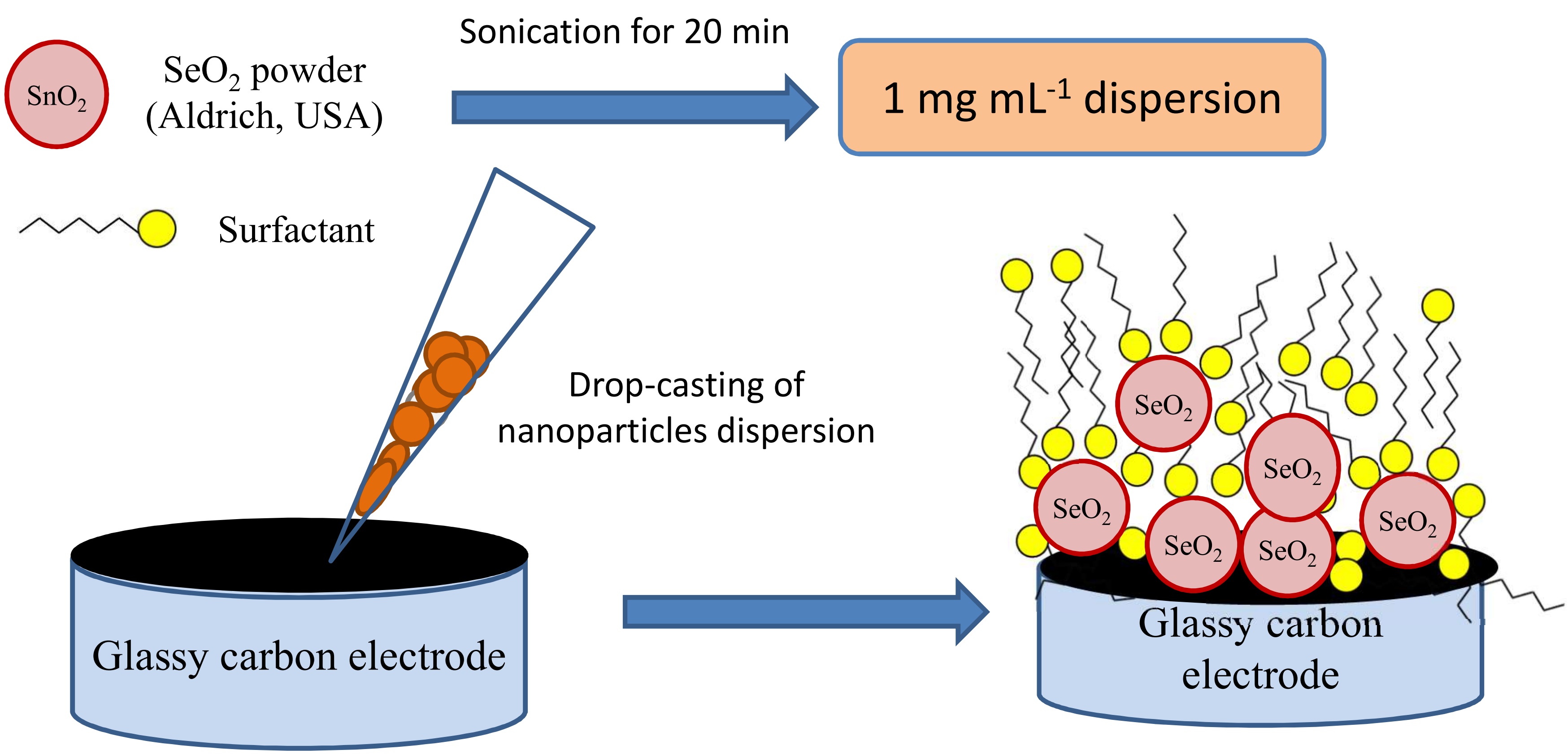
Electrochemical determination of colorants

- ✓ Various types of polarography
- ✓ Voltammetry on traditional electrodes (Pt, glassy carbon)
- ✓ **Voltammetry on chemically modified electrodes**

Non-metal oxide nanoparticles (SiO_2 and SeO_2) are perspective electrode surface modifiers but did not get enough attention

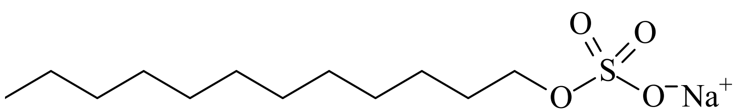
The aim of the work is development of a novel sensitive voltammetric sensors based on the glassy carbon electrode modified with SeO_2 nanoparticles and surfactants for the carminic acid and indigotine determination

Results and discussion

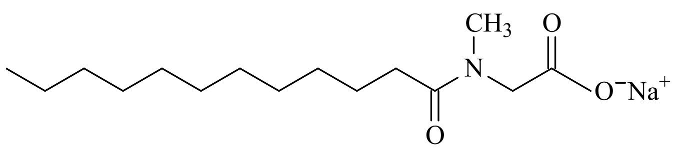


Surfactants

Anionic

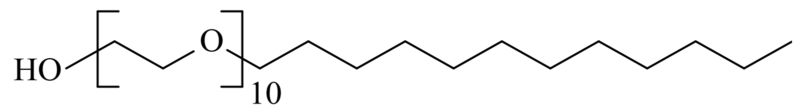


Sodium dodecyl sulfate (SDS)

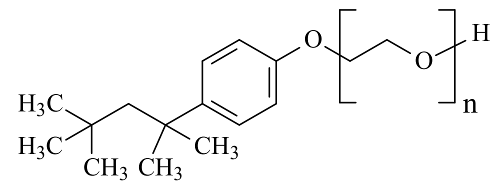


Sodium lauroyl sarcosinate (SLS)

Non-ionic



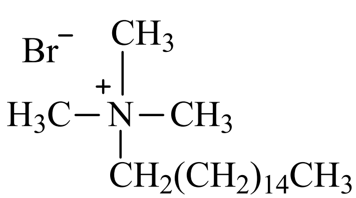
Brij® 35



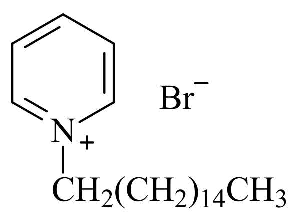
n = 9-10

Triton X-100

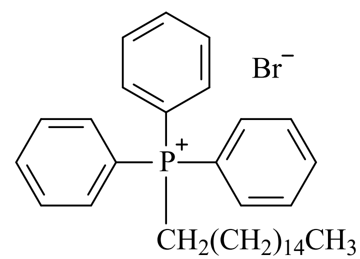
Cationic



Cetyltrimethyl ammonium bromide (CTAB)



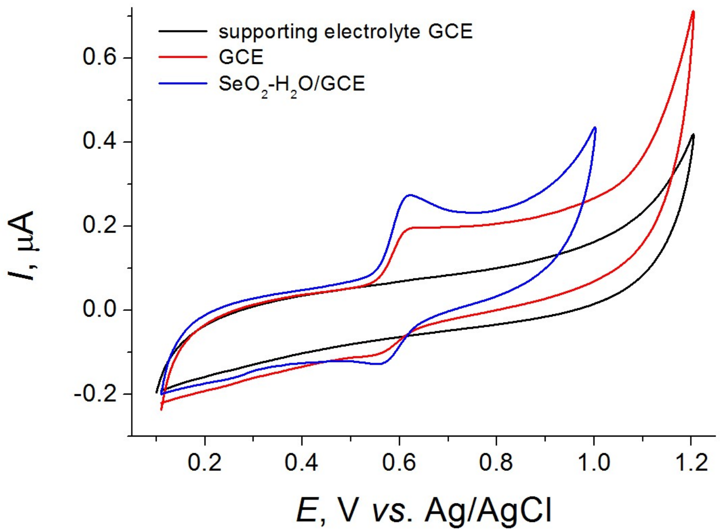
Cetylpyridinium bromide (CPB)



Cetyltriphenylphosphonium bromide (CTPPB)

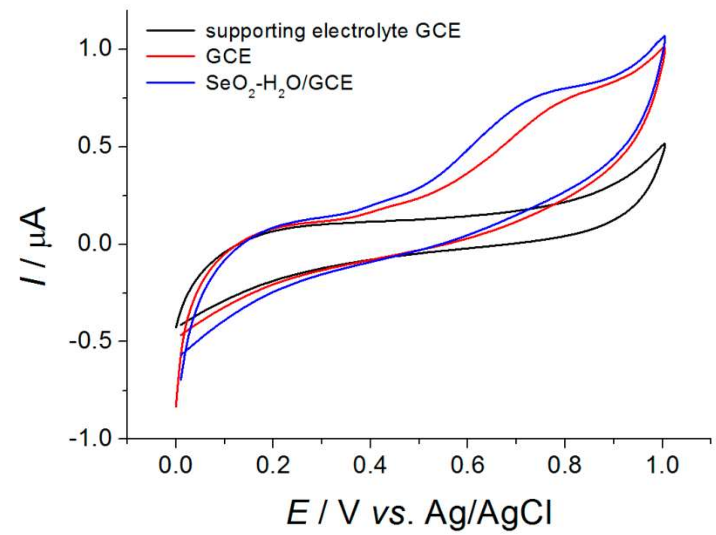
Cyclic voltammetry of colorants at the glassy carbon (GCE) and SeO_2-modified electrodes

10 µM carminic acid



Supporting electrolyte – Britton-Robinson buffer pH 2.0. υ=100 mV/s.

50 µM indigotine



Supporting electrolyte – phosphate buffer pH 7.0. υ=100 mV/s.

Sensitivity of colorants’ response at the modified electrode is still insufficient

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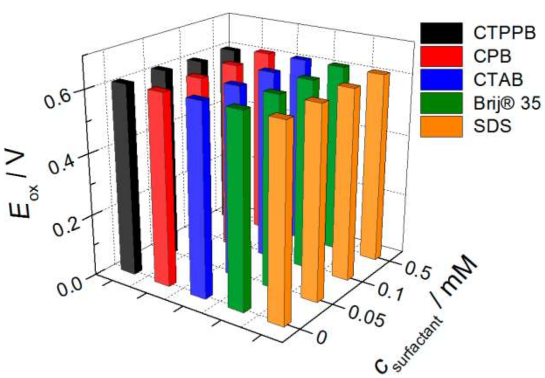
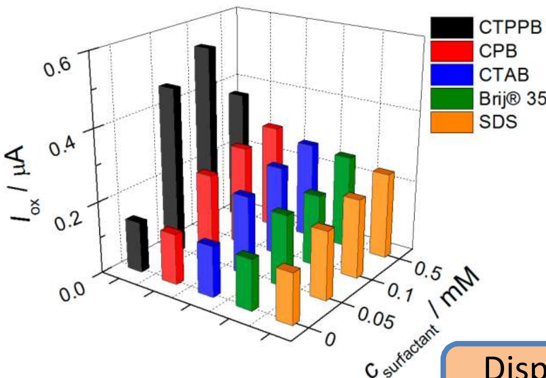
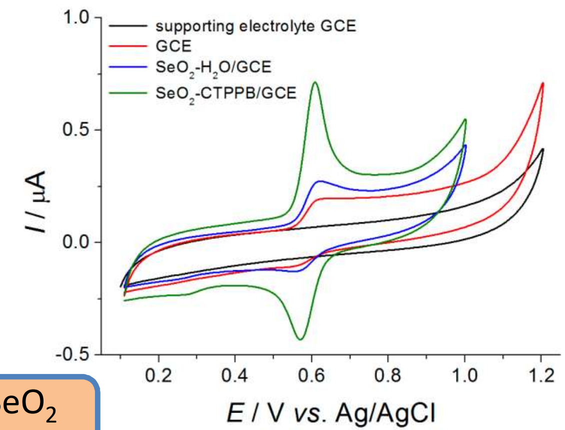
Effect of surfactants nature and concentration in modifier dispersion on the voltammetric characteristics of colorants

10 µM carminic acid

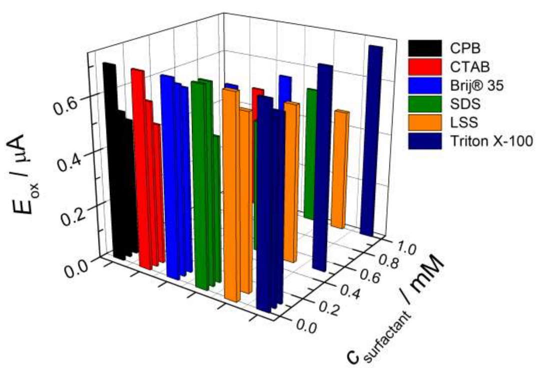


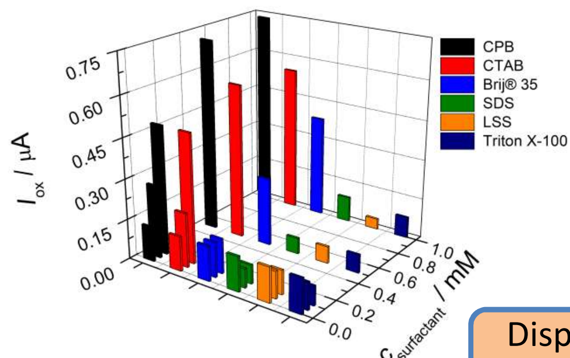


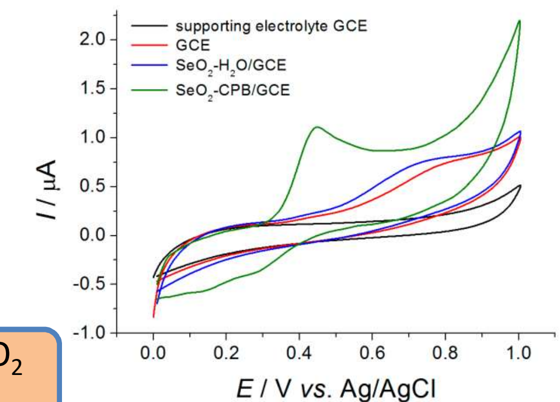


Dispersion of SeO_2 in 0.10 mM CTPPB

50 µM indigotine



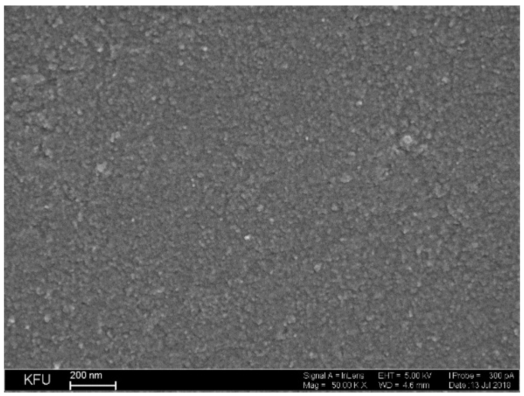




Dispersion of SeO_2 in 1.0 mM CPB

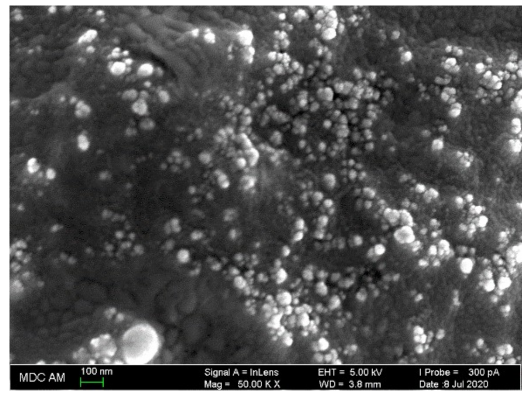
Morphology of the electrode surface based on the scanning electron microscopy data

GCE



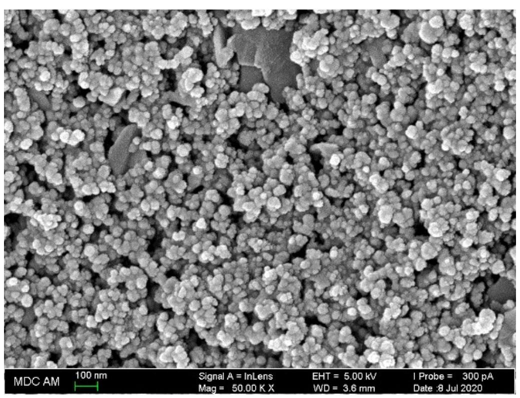
SeO_2-H_2O/GCE

Aggregates of 30-200 nm



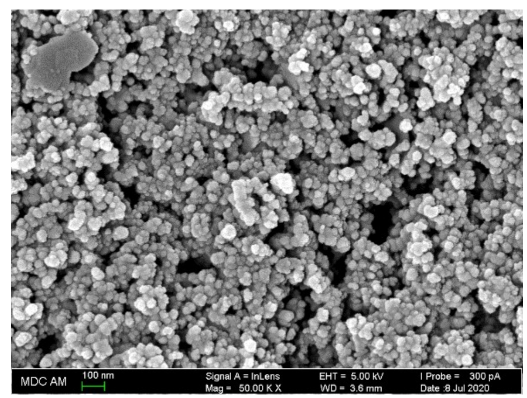
SeO_2-CTPPB/GCE

spheroid nanoparticles of 37-45 nm



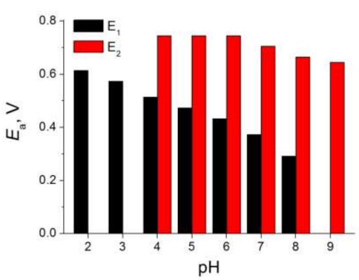
SeO_2-CPB/GCE

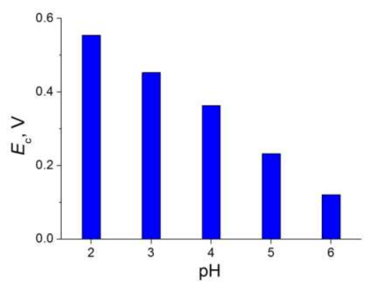
spheroid nanoparticles of 39–55 nm

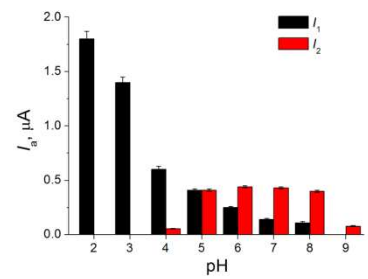


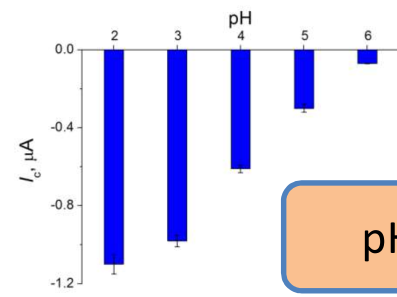
Effect of pH on the voltammetric characteristics of colorants at the SeO_2 nanoparticles modified electrodes

50 µM carminic acid









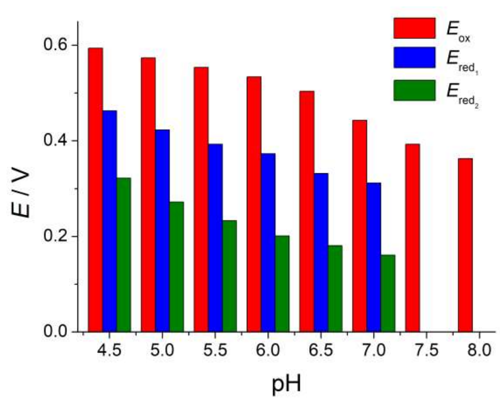
pH = 2.0

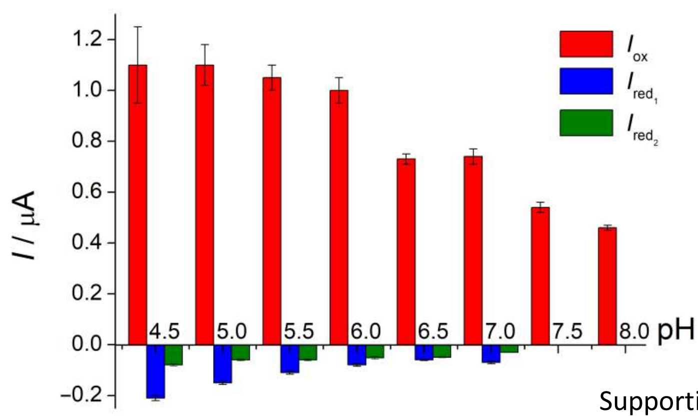
Equal number of electrons and protons on the first step

Supporting electrolyte – Britton-Robinson buffer. υ=100 mV/s.

50 µM indigotine

Protons participate in the oxidation



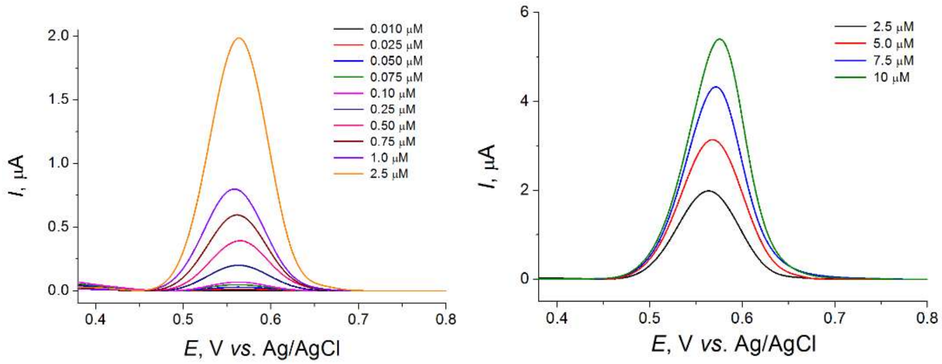


pH = 5.0

Supporting electrolyte – phosphate buffer. υ=100 mV/s.

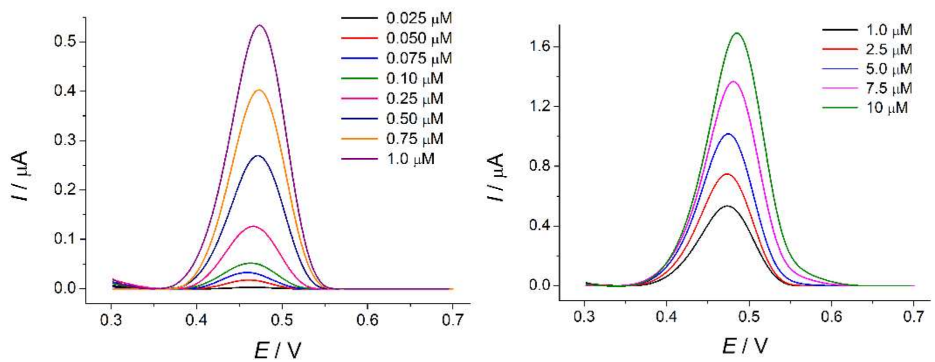
Differential pulse voltammetry of colorants

Carminic acid



Supporting electrolyte – Britton-Robinson buffer pH 2.0. ΔE_{pulse} = 75 mV, t_{pulse} = 25 ms, υ = 10 mV/s.

Indigotine



Supporting electrolyte – phosphate buffer pH 5.0. ΔE_{pulse} = 100 mV, t_{pulse} = 25 ms, υ = 10 mV/s.

Analytical capabilities of the voltammetric sensors

Colorant	Sensor	Detection limit, nM	Linear range, μM
Carminic acid	SeO_2-CTPPB/GCE	3.4	0.010-2.5 and 2.5-10
Indigotine	SeO_2-CPB/GCE	4.3	0.025-1.0 and 1.0-10

Analytical characteristics of voltammetric sensors for the colorants

Sensor	Method	Detection limit, µM	Linear range, µM	Reference
Carminic acid				
Electrodeposition of Pd–Au bimetallic nanoparticles/Polypyroline/Graphite electrode	SWV	0.0059	0.010-1.0	J. Electroanal. Chem., 2016, 760, 32-41.
Polymethionine/Reduced graphene oxide/SPCE	AdADPV	0.036	1-20; 20-60	Molecules, 2021, 26, 2312.
SeO_2 nanoparticles-Cetyltriphenylphosphonium bromide/GCE	DPV	0.0034	0.010-2.5; 2.5-10	This work
Indigotine				
4-(4-Nitrophenilazo)N-benzyl,N-ethylaniline—CPE	DPV	0.36	1–100	Talanta, 2017, 173, 60–68
Polyarginine/CPE	DPV	0.0253	0.2–1.0; 1.5–3.5	J. Electrochem. Sci. Eng., 2021, 11, 87–96.
Polyglycine/CPE	CV	0.011	2–10; 15–60	J. Food Drug Anal., 2018, 26, 292–299.
Chiral amine bis(phenolate) boron complex containing N,N-diethyl-p-phenylenediamine—carboxylated MWNT/GCE	SWV	0.019	0.1–30	Dye. Pigment., 2022, 197, 109921.
SeO_2 nanoparticles—CPB/GCE	DPV	0.0043	0.025–1.0; 1.0–10	This work

Results of voltammetric determination of colorants in model solutions (*n*=5; *P*=0.95)

Colorant	Sensor	Added, µg	Found, µg	RSD, %	*R*, %
Carminic acid	SeO_2-CTPPB/GCE	0.0246	0.025±0.001	3.7	101±3
		0.246	0.245±0.006	2.0	99±2
		1.85	1.85±0.03	1.4	100±1
		12.3	12.3±0.2	1.4	100±1
		24.6	24.6±0.2	0.78	100±1
Indigotine	SeO_2-CPB/GCE	0.0583	0.058 ± 0.001	1.0	99 ± 1
		0.233	0.23 ± 0.01	1.8	100 ± 2
		1.75	1.74 ± 0.03	1.3	99 ± 2
		11.7	11.7 ± 0.3	2.1	100 ± 2
		23.3	23.3 ± 0.2	0.65	99.8 ± 0.8

MDPI

Selectivity of the sensors developed

Interference	Tolerance level	
	Carminic acid (0.10 µM)	Indigotine (0.50 µM)
K^+, Mg^{2+}, Ca^{2+}, NO_3^-, Cl^- and SO_4^{2-} ions	1000-fold excess	1000-fold excess
glucose, sucrose, rhamnose	100-fold excess	100-fold excess
ascorbic acid	1000-fold excess	≤ 10µM
quinoline yellow	—	100-fold excess
riboflavin	—	1000-fold excess
Menthol, aspartame, benzydamine hydrochloride	—	1000-fold excess

Sensors are applicable in pharmaceutical dosage forms analysis

Determination of colorants in real samples (*P*=0.95)

Colorant	Sample Type	№	Labelled amount (mg)	Found by voltammetry (mg)	RSD (%)	Found by spectrophotometry (mg)	RSD (%)	*t*-Test	*F*-Test
Carminic acid	Lozenges for sore throat treatment	1	–	245±6	2.0	249±12	2.0	0.840*	1.04*
		2	–	242±6	2.2	245±17	2.9	0.792*	1.79*
Indigotine	Vitamin tablets		–	0.0047 ± 0.0003	4.4	0.0051 ± 0.0003	4.5	1.97	1.21
	Lozenges for symptomatic local treatment of the mouth and throat	1	0.015	0.0150 ± 0.0004	2.3	0.0148 ± 0.0003	1.5	0.976	2.07
		2	0.031	0.0311 ± 0.0009	2.3	0.0313 ± 0.0009	2.4	0.559	1.12
	Capsules of non-steroidal anti-inflammatory drug		–	0.055 ± 0.002	3.7	0.053 ± 0.002	2.7	1.31	0.810

*t_{crit} = 2.45 at α = 0.05 and f = 6. *F_{crit} = 19.25 at α = 0.05 and f_1= 4, f_2=2.

t_{crit} = 2.31 at α = 0.05 and f = 8. F_{crit} = 6.39 at α = 0.05 and f_1 = f_2 = 4.

Conclusions

SeO_2 nanoparticles dispersed in cationic surfactant media have been shown as an effective sensing layer of the voltammetric sensors for the colorants used in pharmaceutical industry. Indigo carmine and indigotine have been considered as an analytes. 0.10 mM cetyltriphenylphosphonium bromide and 1.0 mM cetylpyridinium bromide have been used as dispersive media for SeO_2 nanoparticles as far as provide the best voltammetric response of carminic acid and indigotine, respectively.

The analytical characteristics of colorants on the sensors developed are the best ones among electrochemical sensors based on various nanomaterials. Simplicity of sensors fabrication, high selectivity and sensitivity of response as well as reliability of the results obtained are the main advantages of the sensors developed. The versatility of the sensors based on the SeO_2 nanoparticles and cationic surfactants functioning under differential pulse voltammetry has been confirmed by direct analysis of the pharmaceutical dosage forms. A good agreement with the independent method data allows consider voltammetric sensors developed as an alternative method for the pharmaceutical products quality control.