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Guaicolic spices curcumin and capsaicin electrochemical oxidation behaviour at a glassy carbon electrode

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ABSTRACT

The electrochemical behaviour of the spice biomarkers, curcumin and capsaicin, two polyphenolic compound with a large spectrum of medical application, has been studied by cyclic, differential pulse and square wave voltammetry at a glassy carbon electrode. The oxidation of curcumin is an irreversible process that in acidic and mild alkaline supporting electrolytes proceeds in two steps. The first irreversible oxidation step leads to the formation of a catechol moiety, and the second reversible step occurs for a higher potential. The oxidation mechanism of ferulic acid, capsaicin and dihydrocapsaicin, curcumin chemical analogues was also investigated. The oxidation of ferulic acid is similar to curcumin whereas the oxidation of capsaicin and dihydrocapsaicin led to the formation of only one oxidation product. A redox mechanism for curcumin oxidation has been proposed.

1. Introduction

Curcumin, 1.7-bis (4-hydroxy-3-methoxyphenyl)-1.6-heptadieno-3,5-dione, Scheme 1A, and capsaicin, 8-methyl-N-vanillyl-6-nonenamide, Scheme 1C, are the major phytochemicals found in some of the most consumed dietary spice ingredients turmeric (saffron) and chili peppers. Besides the flavour and taste that makes these spices very popular especially in Indian and Mexican cuisine, the curcuminoids from saffron and curry are also popular as colouring agents and food dyes, whereas capsaicinoids from chili peppers are particularly appreciated for the pungent action [1–3].

Due to high medicinal potential with virtually no side effects, these compounds have attracted considerable interest in recent years [1–4]. Their therapeutic potential is being explored in inflammatory [5,6], cardiovascular [7,8], neurodegenerative [9,10], neoplasic diseases [11,12], as well as other disorders [13,14]. The presence of the 4-hydroxy-3-methoxy phenyl residue allows them to specifically interact with sensory neurons, and from this point of view, capsaicin has been used to treat peripheral painful conditions and neuropathies [10,15,16]. It was shown that curcumin regulates the classical and the alternative pathway of nervous system, being used in the treatment of Alzheimer, multiple sclerosis and dementia [9,10,17].

In fact, capsaicin and especially curcumin have received considerable attention owing to their antitumor properties, exerting their effects either at the stage of tumorigenesis or in selectively inducing apoptosis in tumor cells [12,18–20].

The complex mechanism of action of curcumin involves various biological targets such as signal transducers and activators, DNA and several kinase enzymes [18–20]. Also, modulation of intracellular redox state is an indirect mechanism since several critical transcription factors control cell cycle, differentiation, stress response and other physiological processes [19–23]. Curcumin has also been shown to potentiate the effect of chemotherapeutic agents [21] and of γ-radiation [22] in cell culture, and capsaicin is able to trigger apoptosis in human cancer cells, and a direct inhibitory effect of tumour growth has been observed [19,23].

The presence of 4-hydroxy-3-methoxy phenyl residue also confers to curcumin and capsaicin, strong antioxidant activity which leads to radical scavenging ability, also useful to prevent cancer and other mentioned diseases [1–6,24,25]. However, as redox agent, they can also act as pro-oxidants thus exhibiting dual effects on carcinogenic and mutagenic processes [25,26]. Such behaviour is determined by the same structural patterns and perhaps is the explanation for all the controversy surrounding epidemiologic studies about the therapeutic use of phytoantioxidants.

The electrochemical characterisation under different conditions is a promising tool to understand the redox behaviour of polyphenolic compounds in physiological medium and several studies are reported on the electrochemical properties of curcumin [27,28 and

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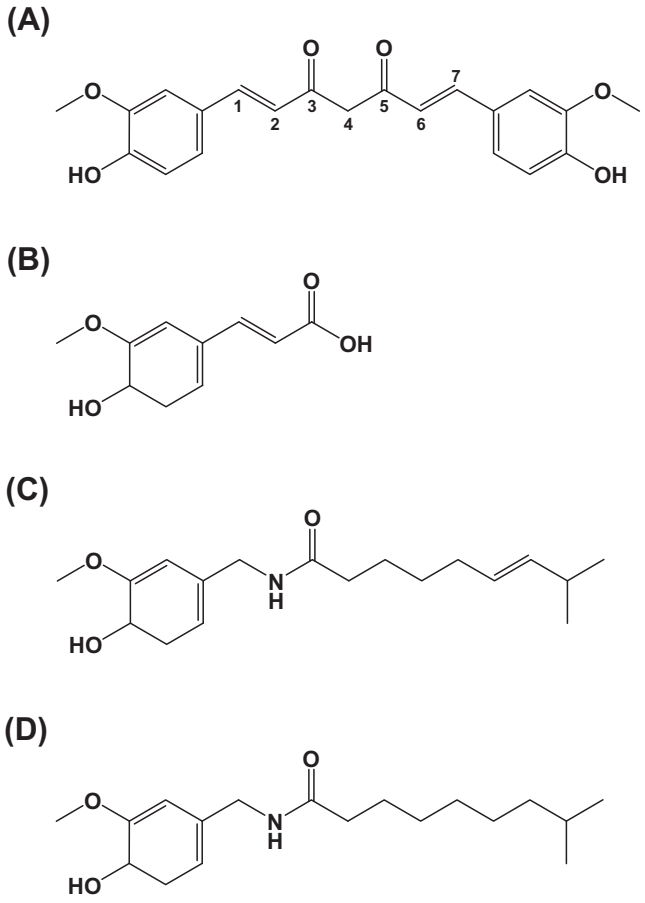

Scheme 1. Chemical structures: (A) curcumin, (B) ferulic acid, (C) capsaicin and (D) dihydrocapsaicin.

references herein] and capsaicin [29] but no study is concerned with the determination of their redox mechanism.

The aim of the present study is to investigate and propose a mechanism for the oxidative behaviour of the curcumin and capsaicin at glassy carbon electrode, using cyclic, differential pulse and square wave voltammetry, in different pH conditions.

The electrochemical behaviour of the chemical analogues ferulic acid and dihydrocapsaicin was also carried out to clarify and support the proposed a mechanism for the oxidative behaviour of the curcumin and capsaicin.

2. Experimental

2.1. Materials and reagents

Curcumin, capsaicin and dihydrocapsaicin from Extrasynthèse (Genay, France) and ferulic acid from Sigma–Aldrich (Spain), were used without further purification. Stock solutions were prepared in ethanol and stored at 4 °C. Solutions of different concentrations of all compounds were prepared by dilution of the appropriate quantity in supporting electrolyte.

All supporting electrolyte solutions [30] were prepared using analytical grade reagents and purified water from a Millipore Milli-Q system (conductivity $\leqslant$0.1 μS cm^{-1}), Table 1.

Table 1
Supporting electrolyte solutions [30].

pH	Composition
1.3	HCl + KCl
2.0	HCl + KCl
3.5	HAcO + NaAcO
4.3	HAcO + NaAcO
6.1	NaH_2PO_4 + Na_2HPO_4
6.9	NaH_2PO_4 + Na_2HPO_4
8.1	NaH_2PO_4 + Na_2HPO_4
9.9	NH_3 + NH_4Cl
12.0	NaOH + KCl

2.2. Apparatus

Voltammetric experiments were carried out using an Autolab PGstat 10 running with GPES 4.9 software, Eco-Chemie, Utrecht, The Netherlands. Measurements were carried out using a three-electrode system in a 0.5 mL one-compartment electrochemical cell (Cypress System Inc., USA). Glassy carbon electrode (GCE, d = 1.5 mm) was the working electrode, Pt wire the counter electrode and the Ag/AgCl (3 M KCl) reference electrode.

The experimental conditions for differential pulse (DP) voltammetry were: pulse amplitude 50 mV, pulse width 70 ms and scan rate 5 mV s^{-1}. For square wave (SW) voltammetry were: pulse of 50 mV, frequency of 10 Hz and a potential increment of 2 mV, corresponding to an effective scan rate of 20 mV s^{-1}, were used.

The GCE was polished using diamond particles of 3 μm (Kemet, UK) before each electrochemical experiment. After polishing, it was rinsed thoroughly with Milli-Q water. Following this mechanical treatment, the GCE was placed in buffer supporting electrolyte and voltammograms were recorded until a steady state baseline voltammograms were obtained. This procedure ensured very reproducible experimental results.

The pH measurements were carried out with a Crison micropH 2001 pH-metre with an Ingold combined glass electrode. All experiments were done at room temperature (25 ± 1 °C) and microvolumes were measured using EP-10 and EP-100 Plus Motorized Microliter Pippettes (Rainin Instrument Co. Inc., Woburn, USA).

2.3. Acquisition and presentation of voltammetric data

All the voltammograms presented were background-subtracted and baseline-corrected using the moving average application with a step window of 2 mV included in GPES version 4.9 software. This mathematical treatment improves the visualisation and identification of peaks over the baseline without introducing any artefact, although the peak intensity is, in some cases, reduced (<10%) relative to that of the untreated curve. Nevertheless, this mathematical treatment of the original voltammograms was used in the presentation of all experimental voltammograms for a better and clearer identification of the peaks. The values for peak current presented in all plots were determined from the original untreated voltammograms after subtraction of the baseline.

3. Results

The anodic oxidation behaviour of curcumin and capsaicin was investigated at a GCE in different experimental conditions using CV, DP and SW voltammetry, over a wide pH range between 1.0 and 12.0. The electrochemical study of ferulic acid and dihydrocapsaicin was also carried out in order to identify the redox active centres of curcumin and capsaicin.

3.1. Cyclic voltammetry

3.1.1. Curcumin and ferulic acid

On the first CV in 500 μM curcumin in pH = 4.3 0.1 M acetate buffer showed the occurrence of two consecutive anodic processes, peak 1_a at E_{p1a} = +0.57 V and peak 2_a, at E_{p2a} = +0.67 V, Fig. 1A.