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Selective voltammetric detection of dopamine in the presence of ascorbate†

Damien W. M. Arrigan,*[a] Mihaela Ghita[b] and Valerio Beni[a]

[a] *NMRC, University College, Lee Maltings, Prospect Row, Cork, Ireland. E-mail: damien.arrigan@nmrc.ie*

[b] *Department of Chemistry, University of Salford, Salford, UK M5 4WT*

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The selective detection of dopamine in the presence of ascorbate is demonstrated based on the voltammetry of dopamine transfer across the interface between two immiscible electrolyte solutions (ITIES) facilitated by an organic-phase ionophore; ascorbate transfer does not occur, leading to highly selective detection of dopamine in the presence of excess ascorbate.

The electrochemical determination of dopamine[1] in physiological samples or *in vivo* is an attractive option from a sensitivity and cost viewpoint.[2] However the determination remains a challenge because of the presence of a large excess of ascorbate.[2] Both compounds undergo two-electron oxidation at commonly used electrode materials and are oxidized at similar potentials. The resultant voltammetric current measurements are completely dominated by the oxidation of ascorbate, whose concentration is in excess over that of dopamine. Various strategies have been employed for alleviation of this selectivity problem, including coupling with chromatographic separation[3] procedures, and modification of electrode surfaces to either shift the oxidation potential[4,5] of either compound away from the other or preventing access of the ascorbate to the electrode surface.[6–8] In the latter case, a common approach is to coat the electrode surface with a cation-permselective thin film which allows access of dopamine (cationic at physiological pH) while excluding ascorbate (anionic at physiological pH). Nafion[6] and other polymeric materials[7,8] have been investigated for such applications. However, it has been found that the oxidized dopamine product, dopamine-*o*-quinone, can mediate in the oxidation of ascorbate at the film/solution interface so that ascorbate interference still occurs. It is also known that the oxidation products of dopamine[9] can adhere to the electrode surface, leading to attenuation of the analytical signal.

Voltammetry at the ITIES[10,11] has been investigated in recent times as a means for the determination of substances not easily oxidised or reduced at electrodes. This approach offers a strategy for the voltammetric determination of ions which is not reliant on oxidation or reduction of the ion but on the interfacial potential-controlled transfer from an aqueous phase to an organic phase (or *vice versa*). Although the facilitated transfer of a range of amines, including dopamine and other biogenic amines, across the ITIES has been reported,[12,13] no examination of the detection of dopamine in the presence of ascorbate at the ITIES has been reported. The oxidation of ascorbate at the ITIES has been reported,[14,15] but not in the context of its interference in the detection of dopamine. In this communication, we report the facilitated transfer of dopamine from water to solvent phase in the presence and absence of ascorbic acid. The transfer of dopamine to the organic phase leads to a current which is not dependent on the oxidation of the dopamine. This means that there is no oxidised dopamine product produced which can react with ascorbate and results in the achievement of excellent selectivity for dopamine in the presence of ascorbate.

Facilitated transfer of dopamine across the ITIES was achieved by use of dibenzo-18-crown-6 (DB18C6) as the organic phase ionophore, which forms a complex with the dopamine by sequestering the protonated amine group within the crown structure. Such transfer, studied by cyclic voltammetry at the ITIES, was achieved with either bis(triphenylphosphoranylidene)ammonium tetraphenylborate (BTPPATPB) or bis(triphenylphosphoranylidene)ammonium tetrakis(4-chlorophenyl)borate (BTPPATCB) as the organic phase electrolyte. Fig. 1 illustrates the voltammetric facilitated transfer of dopamine across the ITIES. By carrying out voltammetric sweep rate experiments with either dopamine or DB18C6 as the excess reagent, it is possible to evaluate the diffusion coefficient of both reagents in their respective phases.

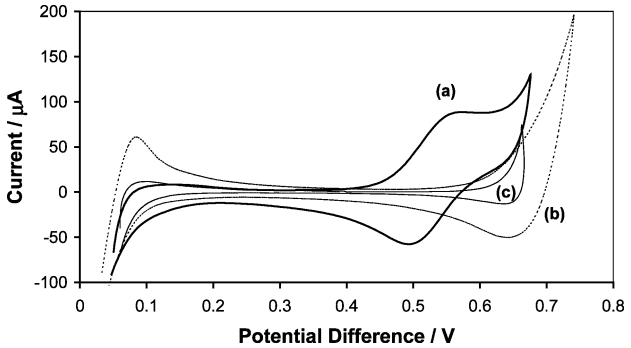

Fig. 1 Cyclic voltammograms illustrating the facilitated transfer of dopamine (a) and no transfer of ascorbate (b) across the ITIES. Organic phase: BTPPATCB (10 mM) and DB18C6 (10 mM) in 1,2-dichloroethane). Aqueous phase: Li_2SO_4 (10 mM). Concentration of dopamine: 0.5 mM; concentration of ascorbate: 10 mM. (c) is the blank voltammogram. Sweep rate: 50 mV s^{-1}.

Table 1 Diffusion coefficients for dopamine in the absence and presence of ascorbate (calculated from the sweep rate dependence of the voltammetric peak currents)

Organic phase electrolyte	$D_{Dopamine}$ / cm^2 s^{-1} (absence of ascorbate)	$D_{Dopamine}$ / cm^2 s^{-1} (presence of ascorbate, 10 mM)
BTPPATPB	10.9 (± 3.9) × 10^{-6}	12.2 (± 2.3) × 10^{-6}
BTPPATCB	6.9 (± 1.3) × 10^{-6}	8.6 (± 1.6) × 10^{-6}

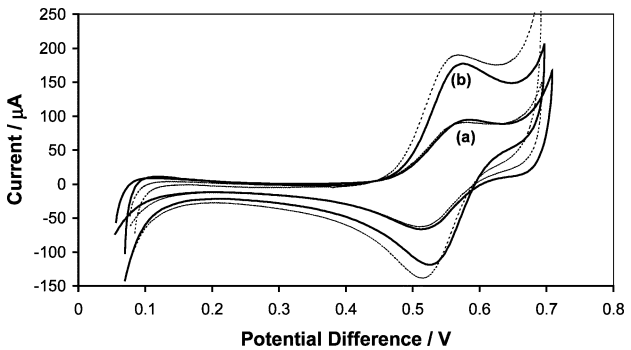

Fig. 2 Cyclic voltammograms illustrating dopamine facilitated transfer across the ITIES at (a) 0.5 mM and (b) 1.0 mM dopamine in the absence (solid lines) and presence (dashed lines) of 10 mM ascorbate in the aqueous phase. Other conditions as for Fig. 1.

† Electronic supplementary information (ESI) available: experimental details, cell compositions, methodology. See http://www.rsc.org/suppdata/cc/b3/b316493d/

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Table 2 Calibration plot data and detection limits for dopamine facilitated transfer using cyclic voltammetry (organic phase: 10 mM BTPPATCB)

Conditions	Range examined/mM	Slope[a]/A M^{-1}	*R*	LOD/mM
No ascorbate in aqueous phase	0.5–1.0 (n = 6)	0.193 (± 0.028)	≥ 0.994	0.13
10 mM ascorbate in aqueous phase	0.5–1.0 (n = 6)	0.194 (± 0.020)	≥ 0.995	0.11

[a] Average and standard deviation of three independent calibration plots.

For the situation where organic phase DB18C6 was in excess over aqueous phase dopamine, the peak currents were proportional to the square root of the voltammetric sweep rate, in the range 5–50 mV s^{-1}, as expected for species freely diffusing to a planar interface. The peak-to-peak separation was *ca.* 60 mV, consistent with the reversible transfer of a singly charged species. These results indicate that the ion transfer of dopamine, facilitated by DB18C6, across the water/1,2-DCE interface is reversible and controlled by the diffusion of dopamine in the aqueous phase. The diffusion coefficients, calculated for different experimental conditions, are shown in Table 1.

In the presence of organic phase BTPPATCB, the diffusion coefficient is in good agreement with that obtained experimentally from solid electrode voltammetry (2.8×10^{-6} cm^2 s^{-1}, determined by voltammetry at platinum or glassy carbon disc electrodes) and with published data: 6×10^{-6} cm^2 s^{-1},[16], 2×10^{-6} cm^2 s^{-1},[13] 7.9 $\times 10^{-6}$ cm^2 s^{-1}.[12] The diffusion coefficient for DB18C6 in the organic phase was determined when the dopamine concentration in the aqueous phase was in excess over the organic phase DB18C6. In this case, the transfer process is controlled by the diffusion of the ionophore to the interface. The diffusion coefficient calculated from the sweep-rate dependence of the peak currents was 1.4 (± 0.14) $\times$ 10^{-6} cm^2 s^{-1} (irrespective of the organic phase electrolyte), in agreement with published values.[17,18]

Under the conditions of this work, ascorbic acid exists in the anionic form. If it crosses the ITIES, the current for transfer in either direction should be the opposite of that for dopamine transfer. Additionally, ascorbate does not posses functionality which complexes with DB18C6 so any transfer would need to be unfacilitated. Fig. 1(b) illustrates that ascorbate does not transfer in the presence of organic phase DB18C6; similar experiments in the absence of organic phase ionophore revealed similar voltammograms signifying neither unfacilitated nor facilitated transfer of ascorbate under the experimental conditions employed here. Addition of ascorbate to a solution of dopamine revealed that the ascorbate had no significant influence on the facilitated transfer of dopamine (Fig.. 2). The diffusion coefficient of dopamine calculated from voltammetric sweep rate experiments was not altered by the presence of excess ascorbate (Table 1).

The influence of ascorbate on the voltammetric transfer of dopamine at the ITIES was further evaluated by assessing the linear detection range and estimation of detection limits for the cyclic voltammetric detection of dopamine in the absence and presence of added ascorbate. Table 2 summarizes the data. Both the slope and the correlation coefficient for the linear calibration plots were unchanged for the concentration range of dopamine examined (0.5–1.0 mM) if excess (10 mM) ascorbate was added. Similarly the detection limit for this detection method was not influenced by the addition of ascorbate. In all of these experimental situations, the ionophore concentration in the organic phase was in excess over dopamine in the aqueous phase. The detection limits obtained with use of organic phase BTPPATPB electrolyte were double those obtained with organic phase BTPPATCB, irrespective of whether ascorbate was present or not.

Further development of this ITIES voltammetry approach to selectivity for dopamine over ascorbate can lead to development of novel voltammetric sensors capable of operating *in vivo* and eventually replacing the carbon-based sensors commonly in use for dopamine and other neurotransmitter determinations. Detection limits, for example, can be greatly improved by use of advanced voltammetric methods (pulse voltammetry, pulse amperometry, stripping voltammetry), incorporation into analytical flow systems as well as exploitation of the benefits of micro-sized ITIES. This provides a great opportunity for selective detection of dopamine in the presence of ascorbate, with potential for applications in a number of biological areas. Selectivity issues over other important biological species remain to be determined. Investigation of novel ionophores[19] with this target in mind is under way.

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