Ion transfer voltammetry of protonized biguanides at a polarized liquid-liquid interface

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The aim of this work was to develop an electrochemical method for the detection of antidiabetic drugs, namely the substituted biguanides metformin (MF, *N*,*N*-Dimethylimidodicarbonimidic diamide), phenformin (PF, 2-(*N*-phenethylcarbamimidoyl) guanidine) and 1-phenylbiguanide (PB, 1-(diaminomethylidene)-2-phenylguanidine). While MF has become one of the most widely prescribed oral glucose-lowering agent for the treatment of type 2 diabetes [1], PF and PB have been withdrawn from the market already before 1980 due to a high risk of lactic acidosis. It is noteworthy that all three compounds are extremely strong bases, which inevitably are present in aqueous solutions in their protonated forms, i.e. as single-charged cations. On the other hand, the protonation opens the possibility of their assaying by the ion transfer voltammetry (or amperometry) at a polarized liquid-liquid interface. Here, we demonstrate that the voltammetric detection of those charged cations is possible at the interface between the aqueous solution containing MF, PF or PB and the room-temperature ionic liquid (IL) membrane composed of highly hydrophobic tridodecylmethylammonium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (TDMATFPB), see ref. 2 for methodology. Fig. 1 shows cyclic voltammograms of the protonated MF, and the linear concentration dependence of the peak current (inset). We shall also demonstrate the extremely high stability of protonized biguanides over the wide range of pH in the aqueous solutions and the possibility to estimate the acid dissociation constants K_{a1} and K_{a2} of their mono- and di-protonated forms.

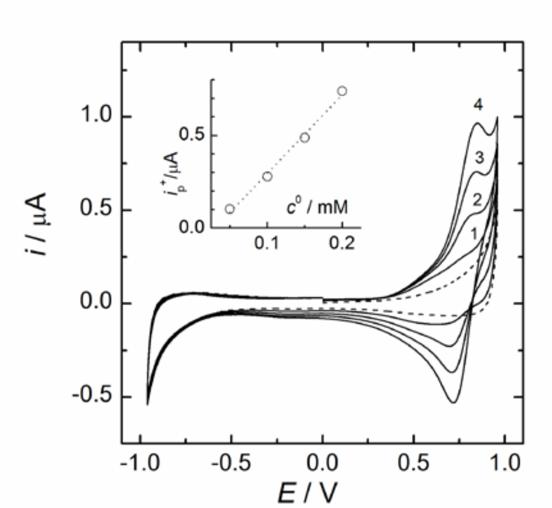

Figure 1. Cyclic voltammograms (10 mV s^{-1}) of a TDMATFPB membrane in the absence (dashed line) and presence (solid line) of metformin at several concentrations (μM): 50 (1), 100 (2), 150 (3), and 200 (4). Inset: Plot of the peak positive peak current i_p^+ vs. the metformin concentration c^0.

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[1] Z. Kender et al., *Exp. Clin. Endocrinol. Diabetes* 2014, **122**, 316-319.

[2] J. Langmaier, Z. Samec, *Anal. Chem.* 2009, **8**, 6382–6389.