



# Effect of charge of quaternary ammonium cations on lipophilicity and electroanalytical parameters: Task for ion transfer voltammetry



Lukasz Poltorak<sup>a,\*</sup>, Ernst J.R. Sudhölter<sup>a</sup>, Louis C.P.M. de Smet<sup>a,b</sup>

<sup>a</sup> Delft University of Technology, Department of Chemical Engineering, Van der Maasweg 9, 2629 HZ Delft, The Netherlands

<sup>b</sup> Wageningen University & Research, Laboratory of Organic Chemistry, Stippeneng 4, 6708 WE Wageningen, The Netherlands

## ARTICLE INFO

### Keywords:

ITIES  
Muscle relaxants  
Partition coefficient  
Gallamine  
Succinylcholine  
Acetylcarnitine

## ABSTRACT

The electrochemical behavior of three differently charged drug molecules (zwitter-ionic acetylcarnitine, bi-cationic succinylcholine and tri-cationic gallamine) was studied at the interface between two immiscible electrolyte solutions. Tetramethylammonium was used as a model mono cationic molecule and internal reference. The charge and molecular structure were found to play an important role in the drug lipophilicity. The studied drugs gave a linear correlation between the water – octanol ( $\log P_{\text{octanol}}$ ) partition coefficients and the electrochemically measured water – 1,2-dichloroethane ( $\log P_{\text{DCE}}$ ) partition coefficients. Comparison with tetraalkylammonium cations indicating that the correlation between  $\log P_{\text{octanol}}$  and  $\log P_{\text{DCE}}$  is molecular structure dependent. The highest measured sensitivity and lowest limit of detection were found to be  $0.543 \text{ mA}\cdot\text{dm}^3\cdot\text{mol}^{-1}$  and  $6.25 \text{ }\mu\text{M}$ , respectively, for the tri-cationic gallamine. The sensitivity for all studied ions was found to be a linear function of molecular charge. The dissociation constant of the carboxylic group of zwitter-ionic acetylcarnitine was calculated based on voltammetric parameters and was found to be 4.3. This study demonstrates that electrochemistry at the liquid – liquid interface is powerful technique when it comes to electroanalytical or pharmacokinetic drug assessment.

## 1. Introduction

Electrochemistry at the liquid – liquid interface or the interface between two immiscible electrolyte solutions (ITIES) is considered as a biomimetic approach [1,2]. This is due to discontinued properties of the liquid – liquid interface that find analogy to lipid membranes in contact with aqueous solutions. Another similarity lies in the ionic transport. ITIES allows studying interfacial ion transfer reactions, as this gives rise to an electric current that can be quantified via a number of electrochemical techniques, including ion transfer voltammetry. Detection – that is not restricted to oxidation and reduction reactions – allows straightforward and direct molecular sensing, which is not always feasible with conventional, solid-state electrodes. Examples include a broad class of molecules containing a quaternary ammonium group (e.g., ionic drugs [3]) or illicit amphetamine drugs, which are inactive at a glassy carbon electrode [4], but do give a signal at the ITIES [5,6]. Furthermore, a list of analytes detectable at electrified liquid – liquid interfaces span of a different class of molecular species. For example, macromolecules, such as dendrimers [7,8], polyelectrolytes [9,10,11] and proteins [12,13] were found to give a characteristic voltammetric behavior indicating interfacial adsorption processes [7,14,15]. Direct

electrochemical detection of alkali and alkaline earth metals from aqueous solutions is also possible [16]. A commonly used methodology involves hydrophobic ionophores dissolved in the organic phase [17,18,19]. The presence of ionophores lowers the standard Gibbs energy of ion transfer from one phase to the other, which is of ultimate interest since alkali and alkaline earth cation transfers are usually hindered by a potential window limiting current or is beyond the available potential window. Ionophores were also used for the detection of inorganic anions, as in the work by Kivlehan et al. where a urea-calix [4]arene was used for phosphate sensing [20]. A lot of attention was given to the interfacial behavior of bio- and bio-relevant molecules as described in a comprehensive review by Arrigan et al. [21].

Besides sensing, electrochemistry at the ITIES plays an increasingly prominent role in pharmacokinetics, especially when it comes to the evaluation of partitioning coefficients ( $P$ , expressed as  $\log P$ ). Such an approach was for the first time proposed by Kontturi and Murtomäki [22] and further developed by others [23,24,25]. As octanol, typically used as a hydrophobic phase, is inappropriate for electrochemical measurements, other solvents like 1,2-dichloroethane (DCE), *ortho*-nitrophenyl *n*-octyl ether (oNPOE) and nitrobenzene (NB) were used [26]. Besides being fast, accurate and relatively easy, current state-of-

\* Corresponding author.

E-mail address: [l.poltorak@tudelft.nl](mailto:l.poltorak@tudelft.nl) (L. Poltorak).



Download English Version:

<https://daneshyari.com/en/article/6477042>

Download Persian Version:

<https://daneshyari.com/article/6477042>

[Daneshyari.com](https://daneshyari.com)