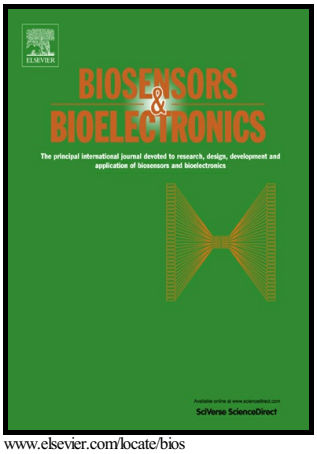
Phenytoin Speciation with Potentiometric and Chronopotentiometric Ion-Selective Membrane Electrodes

Sutida Jansod, Majid Ghahraman Afshar, Gastón A. Crespo, Eric Bakker



www.elsevier.com/locate/bios

PII: S0956-5663(15)30664-3
DOI: http://dx.doi.org/10.1016/j.bios.2015.12.011
Reference: BIOS8241

To appear in: *Biosensors and Bioelectronic*

Received date: 16 September 2015
Revised date: 1 December 2015
Accepted date: 7 December 2015

Cite this article as: Sutida Jansod, Majid Ghahraman Afshar, Gastón A. Crespo and Eric Bakker, Phenytoin Speciation with Potentiometric and Chronopotentiometric Ion-Selective Membrane Electrodes, *Biosensors and Bioelectronic,* http://dx.doi.org/10.1016/j.bios.2015.12.011

Phenytoin Speciation with Potentiometric and Chronopotentiometric Ion-Selective Membrane Electrodes

Sutida Jansod, Majid Ghahraman Afshar, Gastón A. Crespo and Eric Bakker**

Department of Inorganic and Analytical Chemistry, University of Geneva, Quai Ernest-Ansermet 30, CH-1211 Geneva, Switzerland.

Corresponding Authors: eric.bakker@unige.ch; gaston.crespo@unige.ch

Abstract

We report on an electrochemical protocol based on perm-selective membranes to provide valuable information about the speciation of ionizable drugs, with phenytoin as a model example. Membranes containing varying amounts of tetradodecylammonium chloride (TDDA) were read out at zero current (potentiometry) and with applied current techniques (chronopotentiometry). Potentiometry allows one to assess the ionized form of phenytoin (pKa~8.2) that corresponds to a negatively monocharged ion. A careful optimization of the membrane components resulted in a lower limit of detection (~1.6 μM) than previous reports. Once the pH (from 9 to 10) or the concentration of albumin is varied in the sample (from 0 to 30 $g.L^{-1}$), the potentiometric signal changes abruptly as a result of reducing/increasing the ionized concentration of phenytoin. Therefore, potentiometry as a single technique is by itself not sufficient to obtain an information about the concentration and speciation of the drug in the system. For this reason, a tandem configuration with chronopotentiometry as additional readout principle was used to determine the total and ionized concentration of phenytoin. In samples containing excess albumin the rate-limiting step for the chronopotentiometry readout appears to be the diffusion of ionized phenytoin preceded by comparatively rapid deprotonation and decomplexation reactions. This protocol was applied to measure phenytoin in pharmaceutical tables (100 mg per tablet). This tandem approach can likely be extended to more ionizable drugs and may eventually be utilized in view of pharmacological monitoring of drugs during the delivery process.

Keywords: phenytoin, speciation, chronopotentiometry, potentiometry, perm-selective membranes.

1. Introduction