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The Influence of the Receptors Concentration in the Membrane on Its Sensitivity

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Abstract

This paper presents the results of an investigation carried out on some liquid membranes constituted at the interface of an organic medium containing different sodium dipicrilaminate concentrations and an aqueous medium containing various concentrations of some neuropsychotropic substances (ephedrine, lidocaine, mepivacaine and articaine). The study was performed using these membranes as sensors in the construction of ion-selective electrodes for each of the studied substances. The influence of the receptors concentration in the membrane on its sensitivity was investigated relating to the concentration, in aqueous solutions, of the mentioned neuropsychotropic substances. Direct potentiometry at zero current was employed as working technique.

Keywords: cell membrane, ion-selective membrane, direct potentiometry at zero current, dipicrilamine, ephedrine

Introduction

Having in mind the structural and functional similarities between the cell membrane and the artificial ion-selective ones [1-3], there have been investigated some punctual aspects regarding the electrochemical behaviour of the artificial membranes, in order to get some information that could be useful to clear up the interface phenomena mechanisms.

From this point of view an important aspect to be investigated is the influence of the concentration of a certain category of receptors in a membrane on the membrane sensitivity relating to the given chemical species, in the adjacent medium.

In order to establish such an influence there have been studied some artificial membranes formed at the interface between an aqueous medium containing different concentrations of some neuropsychotropic substances [4] such as: ephedrine, lidocaine, mepivacaine and articaine (subsequently noted with X) and a liquid organic medium containing different concentrations of sodium dipicrilaminate (DPA^-Na^+) as the pair substance for them.

When they approached the present study, the authors started from the idea that adsorption processes play an important role in the electrochemical behaviour of the artificial ion-selective membranes by facilitating the formation of charge transfer molecular complexes of DPA^-X^+ type, at the membrane level [1].

As an electron donor, DPA^- forms charge transfer molecular complexes with some monovalent cations as electron acceptors [10]. The cations resulted from the dissociation, in water, of each of the mentioned neuropsychotropic substances (X) hydrochlorides are among the species that form more or less stable charge transfer complexes with DPA^-.

At the level of membranes, as they are constituted in the above-mentioned manner, the DPA^- particles play the role that the pharmacological receptors play in the cell natural membrane [1-3]. This is why from now on, in this paper the term receptor will be used to designate a DPA^- particle too.

Electrochemically, the formation of the DPA^-X^+ charge transfer complexes at the interface of two immiscible media can be monitored selectively by different means, those of the potentiometry at zero current included [1,2,7,8]. In this respect, the membranes that are the object of the present study have been used as sensors in the construction of some ion selective electrodes. The changes in the potential magnitude of such electrodes vs. the saturated calomel electrode (SCE) [1] were investigated relating to the different aqueos concentrations (10^{-6} - 10^{-2} M) of studied X neuropsychotropic substances hydrochlorides.

Materials and Methods

Membrane preparation

Solutions in n-octanol of analytical purity have been prepared 10^{-2} M, $5\cdot10^{-3}$ M, 10^{-3} M, $5\cdot10^{-4}$ M and 10^{-4} M DPA (Merck). Each of these organic solutions was used to fill a previously prepared liquid membrane electrode.

For each studied neuropsychotropic substance X there have been prepared a series of aqueous solutions with concentrations in the 10^{-6} - 10^{-2} M ranges. The constant ionic strength of these solutions was ensured by a 10^{-2} M CH_3COONa concentration. The neuropsychotropic substances used for the aqueous solutions preparation were of pharmaceutical purity.

The membranes, which are the object of this study, are formed at the interface between the aqueous and the organic phases, which the above-mentioned composition.

Measurements

An electrochemical cell (1) using a SCE as reference electrode [9] was used to measure the membrane potential changes.

Internal reference electrode	DPA^-Na^+ solution in n-octanol	Membrane	Aqueous solution of the species X^+	External reference electrode	(1)
(I)	(II)	(III)	(IV)	(V)	

Results

According to Henry adsorption isotherm the concentration level of a certain chemical species in the surface layer of a given phase is directly proportional to the concentration of the same species inside the phase it comes from. This means that the concentration level of the species X^- at the interface (i.e. compartment III) is proportional to the concentration of the species X^- substance inside compartment IV. Consequently, the receptors' concentration at the same interface will be directly proportional to the concentration level of DPA^- inside compartment (II) of the cell (1).

Theoretically, the electromotive force, E, of the cell (1), relating to the concentration of a monovalent species X, active at the membrane level, is given by the Nernst equation:

$$E = E_0 + 0{,}0589 \lg [X] \quad (2)$$

In order to establish the influence of the receptors concentration in the membrane on its sensitivity, the amplitude of the changes in the electromotive force (E) of the cell (1), as a function of species X^- concentration level (10^{-6}-10^{-2}M), in compartment (IV), was investigated for each of the five concentration levels of the receptors (DPA^-) in the membrane.

The measurements carried out using the cell (1) for ephedrine, lidocaine, mepivacaine and articaine pointed out a quite similar electrochemical behaviour of the membranes in relation with the aqueous solutions of all these neuropsychotropic substances. This is a proof that the action mechanism of ephedrine, lidocaine, mepivacaine and articaine on the DPA^- receptors in the membrane is the same. Only the amplitude of the potential changes is different for each of the studied substances under the same working conditions, due to the difference in the affinities between the DPA^- receptors and each of the X^+ species, in the process of DPA^-X^+ charge transfer complex formation at the interface. These results should also be put in connection with the fact that all the studied X^+ species are known as stimulants at the nervous system level (i.e. with similar activity at the level of a certain category of receptors in the neuronal membrane).

As the results of the measurements carried out for articaine aqueous solutions in compartment (IV) of the electrochemical cell (1) with compartment (II) containing one by one the five above mentioned DPA^- concentration levels, in n-octanol, are more relevant for the purpose of the present study, the results are presented graphically in **Figure 1**.

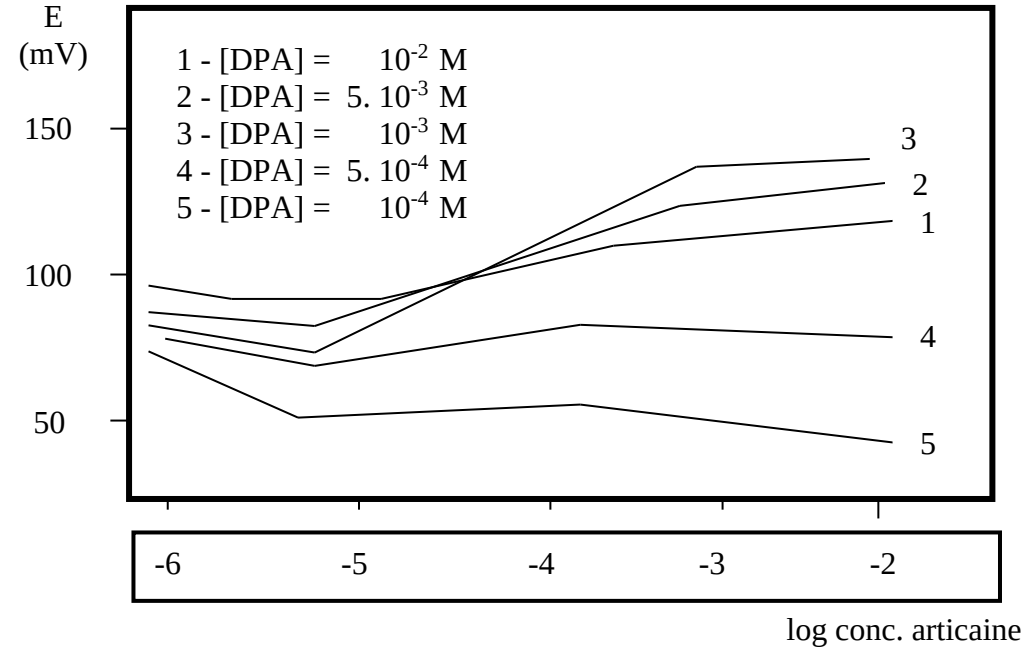

Figure 1. Graphic representation of the electric potential of an ion-selective membrane containing DPA^- ions as receptors, as a function of the articaine concentration in the aqueous medium, for different concentration levels of the receptors in the non-aqueous phase.

Discussions

The results of the measurements point out a quite visible analogy between the phenomenology of the processes that take place at the level of the studied membrane (as well as at the level of the neuronal membrane) and adsorption processes at the interface.

So, it could be seen that the DPA^- receptors in the studied membranes could be considered as binding places on an adsorption surface, and the particles of the species X^+, as

the adsorbed species. Analysing the above-mentioned results, as they appear in **Figure 1**, one can conclude on the following*:*

-The slope of the answering curve of the membrane for the species X^+ (whose concentration level is maintained constant in the aqueous phase) with the decreasing of the concentration level of the DPA^- receptors in the membrane is a direct consequence of the fact that the proportion of the occupied receptors (out of the total initially available receptors) by the particles of the species X^- molecules, increases with the decrease in the initial number of the available receptors, as binding places.

-The minimum concentration level of the species X^-, the membrane answers to, is lowering with the diminishing to a certain level, of the concentration level of the receptors in the membrane.

Thus, it could be concluded that the lowest limit of the concentration level of the species X^+, able to generate a minimum perceivable change in the membrane potential (the "detection limit" in the case of the ion-selective membranes and the "release dose" in the case of the cell membrane in contact with a drug substance) decreases with the diminishing, to a certain level, of the receptors concentration in the membrane.

The easiness and the rapidity of such systems evolve towards an energetic equilibrium state as a function of the receptors concentration in the membrane and/or of the concentration of the species X^- in the aqueous solution [2] should be also, taken into consideration to explain the results above.

The role of membrane receptors concentration in the development of the membrane electrochemical properties (including the formation and the dynamics of the membrane potential) proves to be very important.

Some common elements of, both the Langmuir type adsorption, and the cell membrane phenomena, have been previously identified by some researchers in the pharmacology field, during their studies on the kinetics of the drug-cell membrane interactions, but a consistent and durable theory on this topic was not yet developed.

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