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Determination of tetracyclines by potentiometry using E.I.S. ☆

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Abstract:
Ion-selective electrodes have gained wide applicability in pharmaceutical analysis and the specialized literature also presents some data on their use in the determination of tetracyclines. Ion-selective electrodes for tetracycline were constructed using different electroactive materials and their performances were studied. These electrodes were tested for the determination of these tetracyclines in commercially available tablets. Tetracyclines form a homogeneous class of broad-spectrum antibiotics whose name derives from the tetracyclic structure of the common skeleton, octahydronaphthacene.

Keywords: tetracyclines, ion-selective electrodes, electroactive material. PVC, DOP, dipicrylamine

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1. INTRODUCTION

The most important natural representatives of the tetracyclines were discovered within a few years: chlortetracycline - 1948, oxytetracycline - 1950, and tetracycline - 1953. Later, a series of semi-synthetic products were also obtained [1]. With metal ions, tetracyclines produce chelates that can be used in their purification and separation, in their identification and dosage. It also seems that the pri-oxy-carbonyl structures bind very easily and stably the essential trace elements for the development of microorganisms.

This is probably the mode of action against pathogens. Binding of metal cations deprives them of their use in enzyme production by tetracycline-sensitive microorganisms, the antibacterial activity depending on the efficiency of depletion of trace elements in the environment.

Tetracyclines are solid, crystalline substances, with a golden yellow color, having chromophore groups in the molecule, and have a bitter taste. The solubility in water is reduced, by increasing the pH (greater than 8.5) they become much more soluble. They dissolve in some organic solvents and are very slightly soluble in ether.

Their salts (e.g. hydrochlorides) have higher solubility in water, but lower solubility in some organic solvents (ether, chloroform, acetone). They are optically active substances. They are photosensitive to light, generally turning brown when exposed to light.

The chemical properties characteristic of these substances have been found to be due to both the basic naphthacene nucleus, a higher polynuclear hydrocarbon with linearly condensed nuclei, and the functional groups grafted onto this nucleus, whose chemical character gives tetracyclines an amphoteric character.

Tetracyclines have both an acidic character due to the phenolic group to which is added the acidity of the enolic group, and a basic character imparted by the secondary amine group [2,3]. So tetracyclines are compounds with amphoteric character, a character manifested by the tendency to form salts with both acids and bases under appropriate reaction conditions.

2. MATERIALS AND METHODS

a) Electrode manufacturing

Particular importance in the manufacture of the electrode was given to the creation of the Ag/AgCl internal reference electrode, which was obtained by electrothermal deposition at 600 °C of an AgCl layer on the silver wire.

b) Membrane manufacturing

1. A quantity of 0.2196 g of DPA is dissolved in 25 mL of tridistilled water; the solution is adjusted to pH = 8 by adding NaOH; the appropriate amount of Ox^+Cl^- is added to form the brick-red Ox-DPA complex. The precipitate is filtered under vacuum and dried in an oven for three hours.

2. 0.1001 g of Ox-DPA complex were dissolved in 0.5005 g of DOP, then 0.4004 g of PVC and 5 mL of THF were added.

Solution 2 is introduced into glass rings fixed on a glass surface and left to evaporate for 72 hours. After evaporation, an elastic membrane is obtained on the respective rings from which a corresponding surface is detached and fixed with a suitable adhesive chosen, then the electrode body is filled with an internal solution that ensures electrical contact between the membrane and the internal reference electrode. Then the membrane is left in a 10^{-3} M tetracycline hydrochloride solution for 3 hours for preconditioning. In Fig. 1 a schematic representation of the construction of the oxytetracycline ion-sensitive electrode is shown.

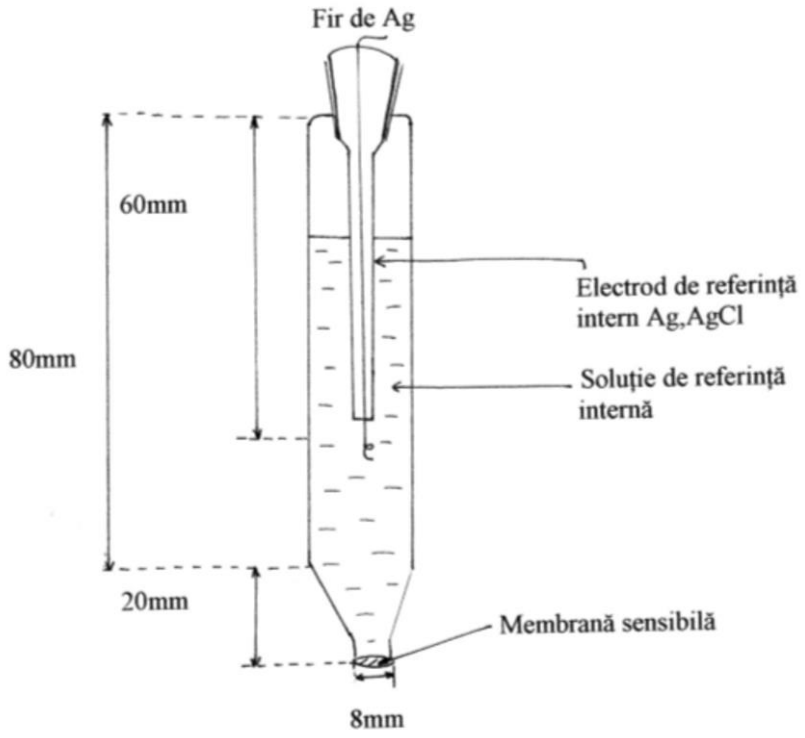

Figure 1. Schematic representation of the construction of the oxytetracycline ion-sensitive electrode.

3. RESULTS AND DISCUSSION

To characterize an EIS, certain parameters must be determined and monitored: response time, linearity range, accessible potential range, detection limit, selectivity, pH influence.

In order to determine the selectivity coefficients for mono- and divalent cations and compounds with similar structure, the voltage of an electrochemical cell containing only the solution of the $OxTe^+$ ion, E1, is measured, then the voltage of a solution containing only the interfering ion Z^{z+}, at a concentration equal to that of $OxTe^+$ in the previous solution (E2), is measured [7,9]. The obtained results are presented in Tables 1, 2, and 3, and in Figs. 2 and 3.

Table 1. Values of electrode potential I as a function of time (determination of response time).

No. crt.	**Time (s)**	**E (V) vs Ag, AgCl**			
		$1 \cdot 10^{-2}$ M OxTe	**$1 \cdot 10^{-3}$ M OxTe**	**$1 \cdot 10^{-4}$ M OxTe**	**$1 \cdot 10^{-5}$ M OxTe**
1	0	0.000	0.000	0.000	0.000
2	30	-0.025	0.000	+0.025	+0.051
3	60	-0.026	0.000	+0.027	+0.053
4	90	-0.027	0.000	+0.028	+0.054
5	120	-0.027	0.000	+0.028	+0.054
6	150	-0.027	0.000	+0.028	+0.054
7	180	-0.027	0.001	+0.028	+0.054
8	210	-0.028	+0.001	+0.028	+0.054
9	240	-0.028	+0.001	+0.028	+0.055
10	270	-0.028	+0.001	+0.029	+0.055
11	300	-0.028	+0.001	+0.029	+0.055
12	330	-0.028	+0.001	+0.029	+0.055
13	360	-0.028	+0.001	+0.029	+0.055

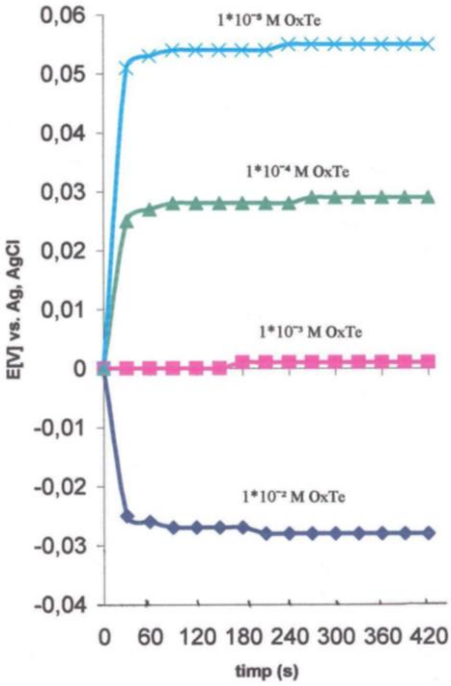

Figure 2. Variation of electrode potential I over time. Stability of response time.

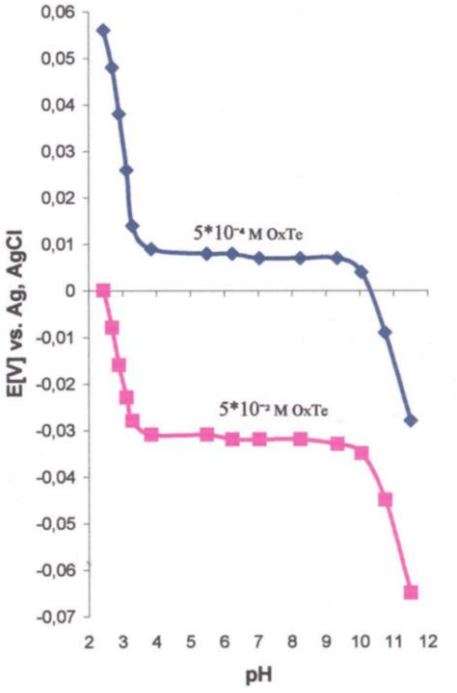

Figure 3. Variation of electrode voltage I depending on solution pH.

The results reveal that the ion-selective oxytetracycline electrode exhibits good selectivity towards mono- and divalent cations and $(CH_3)_4N^+$, but is not selective towards similar compounds.

EIS with a sensitive membrane for OxTe have proven to have good results in analytical determinations, possessing a quasi-linear response with a good response slope value, a response linearity range of 3 decades of concentration (10^{-2} - 10^{-5}) M and especially being selective for a series of mono- and divalent cations studied [10,11].

Table 2. Cell voltage values depending on solution pH for electrode I.

No. crt.	pH solution	E[V] vs. Ag, AgCl	
		$5 \cdot 10^{-4}$ mol/L OxTe	$5 \cdot 10^{-2}$ mol/L OxTe
1	2.45	+0.056	0.000
2	2.70	+0.048	-0.008
3	2.90	+0.038	-0.016
4	3.12	+0.026	-0.023
5	3.30	+0.014	-0.028
6	3.85	+0.009	-0.031
7	5.50	+0.008	-0.031
8	6.25	+0.008	-0.032
9	7.05	+0.007	-0.032
10	8.25	+0.007	-0.032
11	9.35	+0.007	-0.033
12	10.05	+0.004	-0.035
13	10.75	-0.009	-0.045
14	11.5	-0.028	-0.065

Table 3. Values of potentiometric selectivity coefficients for oxytetracycline ion-selective electrodes obtained by the separate solutions method.

Interfering species	K_{pv}/y^{z+pot}
Li^+	0.000470
Na^+	0.000680
K^+	0.000655
Rb^+	0.000720
NH_4^+	0.000643
Ca^{2+}	0.000055
Mg^{2+}	0.000042
Cd^{2+}	0.000036
Pb^{2+}	0.000028
Mn^{2+}	0.000210
Fe^{2+}	0.000095
Co^{2+}	0.000032
Ni^{2+}	0.000180
Cu^{2+}	0.000055
Zn^{2+}	0.000075
Tetraciclină	7.566
Minociclină	6.889
Doxiciclină	6.565
$(CH_3)_4N^+$	0.000750

4. CONCLUSION

A particular advantage of electrodes of this type is that, prepared in laboratories that perform analytical control of oxytetracycline hydrochloride either as the active substance itself or under various forms of conditioning, the electrodes can be ready for use only 4 hours after conditioning.

REFERENCES

[1] C. Daescu, Chimia si tehnologia medicamentelor, Ed. Did. si Ped., Bucuresti, p.64, 1994.
[2] *** FarmacopeeaRomana, Ed. Medicala, Bucuresti, p. 354, 1993.
[3] Farmac. Uffic. della Republica Italiana, vol II (nouvoedizione), Roma, Italy, 1993.
[4] Farmac. Francaise Ed.X, Paris, France, 1986.
[5] I. Ganescu, I. Papa, Anca Ganescu, L. Chirigiu, Rev. Chim.(Bucureşti), 51(9)(2000), 697.
[6] I. Ganescu, Al. Popescu, L. Chirigiu, I. Papa, Anal. Univ. Buc., seria Chimie, VII(1998), 33
[7] I. Ganescu, I. Papa, Anca Ganescu, L. Chirigiu, Viorica Popescu, Farmacia, 4(2000), 71.
[8] I. Gănescu, Anca Gănescu, G. Brătulescu, Acta Chimica Slovenica, 49(2002), 181.
[9] I.Gănescu, Anca Gănescu, I. Papa, Dan Preda, L. Chirigiu, Alin Barbu, Rev.Chim (Bucureşti) (2001), 52, 6.
[10] Al. Popescu, I.Tănase, Anca Gănescu, Andreea Popescu, Rev.Chim (Bucureşti), 57(2006), 10.
[11] Maria Pleniceanu, Mihaela Mureseanu, I. Ganescu, Olimpia Rusu, J. Indian Chem. Soc., 40(A)(2001), 486.