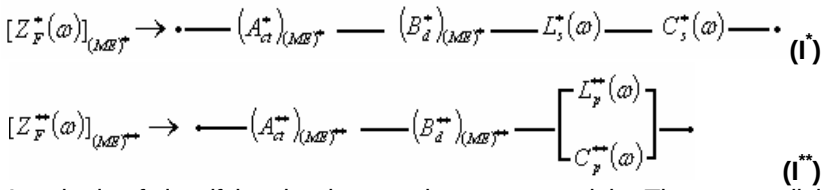
STUDIA UNIVERSITATIS BABEŞ-BOLYAI, CHEMIA, LIV, Sp.Iss. 1, 2009

METHOD OF CLASSIFYING THE DRUGS BY USING THE NYQUIST PLOTS OF A REFERENCE REDOX DIELECTRODE (RRD) AND OF THE MULTIELECTRODE $(ME)_D$=(RRD) CONTAINING THE DRUG D

NICOLAE BONCIOCAT[a] AND ADINA COTARTA[a]

ABSTRACT. The proposed method uses a *reference redox dielectrode* (RRD) in whose electrical scheme enter: the Faraday impedance $[Z_F(\omega)]_{RRD}$ in parallel with the double layer capacity C_d, and the solution resistance R_{sol}. In $[Z_F(\omega)]_{RRD}$ enter in series: the *charge transfer* $(A_{ct})_{RRD}$ and the *diffusion* $(B_d)_{RRD}$ resistances, and the *Warburg* pseudo-capacitance $C_W(\omega)$, ω being the radial frequency of the current. In the multielectrode $(ME)_D = (RRD)$ containing the drug, C_d and R_{sol} maintain their values. To account for the change of $[Z_F(\omega)]_{RRD}$, we have considered *two theoretical quantities*: a *pseudo-capacitance* and a *pseudo- inductance*, and two possible arrangements of them: *in series*, respective *in parallel*. Consequently, other two Faraday impedances have resulted: $[Z_F^*(\omega)]_{(ME)_D^*}$ containing the series arrangement of $L_s^*(\omega)$, $C_s^*(\omega)$, respective $[Z_F^{**}(\omega)]_{(ME)_D^{**}}$ containing the parallel arrangement of $L_p^{**}(\omega)$, $C_p^{**}(\omega)$:



(I*)

(I)**

As criteria of classifying the drug, we have proposed the Thomson radial frequencies $\omega_{Th,s} = [L_s(\omega) \cdot C_s(\omega)]^{-1/2}$, respective $\omega_{Th,p} = [L_p^{**}(\omega) \cdot C_p^{**}(\omega)]^{-1/2}$. Three classes of drugs have resulted: the class(1) of drugs *having no effect*, for which $\omega_{Th,s} = \infty$ and $\omega_{Th,p} = 0$; the class (1*) of drugs *having effect*, for which $\omega_1 < \omega_{Th,s} < \infty$ and the class (1**) of drugs *having effect*, for which $0 < \omega_{Th,p} < \omega_1$. By ω_1 is denoted the smallest radial frequency used.

Keywords: multielectrode, electrochemical impedance spectroscopy, Thomson radial frequencies, drugs classification

[a] *University Politehnica of Bucharest, Department of Applied Physical Chemistry and Electrochemistry, Computer Aided Electrochemistry Laboratory, 1 Gh. Polizu Street, Bucharest 011061, Romania, PO BOX 12- 112, e-mail: c_adina1@yahoo.fr*

INTRODUCTION

In a series of papers, Bonciocat et al., have shown that the faradaic current density of an electrode redox reaction occuring with combined limitations of charge transfer and nonstationary, linear, semiinfinite diffusion is the solution of an integral equation of Volterra type[1-7]. By solving this integral equation, new methods of direct and cyclic voltammetry, applicable in aqueous electrolytic solutions, or in molten salts, have been developed [8-20]. The above mentioned equation has also led to a new approach to the Electrochemical Impedance Spectroscopy when only the charge transfer and diffusion limitations are present[21-23]. Very recently has been shown that the (E I S) method may have important applications in drug research[24-27].

The proposed (E I S) method of classifying the drugs uses the following *reference redox dielectrode*(RRD):

$$Pt|\ [Fe(CN)_6]^{3-} / Fe(CN)_6]^{4-}, KCl\ (in\ excess),\ O_2\ physically\ dissolved \tag{1}$$

which, e.g., in weak acidic media, has the reactions:

$$\frac{1}{4}O_2 + H^+ + e \rightarrow \frac{1}{2}H_2O \tag{1a}$$

$$\left[Fe(CN)_6\right]^{4-} \rightarrow \left[Fe(CN)_6\right]^{3-} + e \tag{1b}$$

Concerning the electric scheme of the measuring cell needed to obtain the Nyquist plots, it refers only to the electrode under study, because the impedance of the reference electrode is practically equal to zero. In an oversimplified scheme, but adequate for the aim of this paper, must enter the *Faraday impedance* Z_F in parallel with the double layer capacity C_d and in series with this parallel arrangement the solution resistance R_{sol} .

As for Z_F, it represents the impedance of a series circuit, in which enter: the *charge transfer resistance* A_{ct}, the *Warburg diffusion resistance* $R_W(\omega)$, and the *Warburg pseudo-capacitance* $C_W(\omega)$, ω being the *radial frequency* of the alternating current [see figure 1].

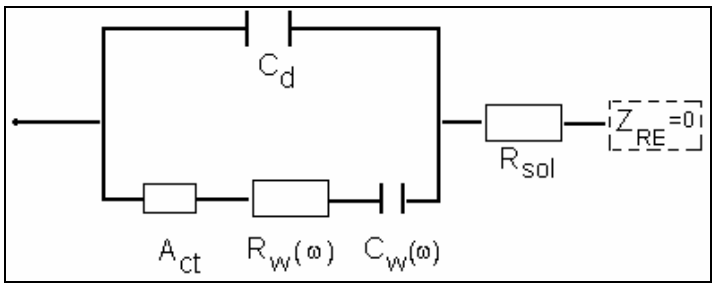


Figure 1. The electric scheme of the measuring cell nedeed to obtain the Nyquist plot of the RRD dielectrode

$C_W(\omega)$ has been introduced by Warburg to explain the phase difference between the current and the tension. A_{ct} and $R_W(\omega)$ are *ohmical terms* which don't introduce a phase difference between the current and the tension, and for this reason, in the complex plane, their values represent the lengths of two segments situated along the *real axes*. $C_W(\omega)$ introduces a *Warburg capacitive reactance* $X_{C_W}(\omega)$, situated along the *imaginary* axes and having the expression:

$$X_{C_W}(\omega) \cong -R_W(\omega)\, j \tag{2}$$

Taking into account the relation that exists between a capacitance C and its capacitive reactance X_C, i.e., $C = 1/\left[\omega |X_C|\right]$, it follows:

$$C_W(\omega) = 1/\left[\omega R_W(\omega)\right] \tag{2'}$$

and thus:

$$\boxed{R_W(\omega) C_W(\omega) = \frac{1}{\omega}} \tag{3}$$

Because the reactions (1a and 1b) occur simultaneously, with *their individual contributions,* it follows that the quantities A_{ct}, $R_W(\omega)$ and $C_W(\omega)$ may be written in the forms:

$$\frac{1}{A_{ct}} = \frac{1}{A_{ct1}} + \frac{1}{A_{ct2}}; \qquad \frac{1}{R_W(\omega)} = \frac{1}{R_{W_1}(\omega)} + \frac{1}{R_{W_2}(\omega)};$$
$$C_W(\omega) = C_{W_1}(\omega) + C_{W_2}(\omega) \tag{4}$$

taking into account the fact that the corresponding resistances and pseudo-capacitances are arranged in parallel.

The figure1 has been considered adequate for the *reference redox dielectrode* (RRD), because the expressions of the Nyquist plots in the domain of very small values of ω, obtained on its basis, have proved to be in good agreement with the experimental data.

THEORETICAL SECTION

The theoretical development given in this paper is based on the following idea: to explain the phase difference between the current and the tension, we shall use instead of *one theoretical quantity* (as the *Warburg pseudo-capacitance* $C_W(\omega)$, *two theoretical quantities*, namely a *pseudo-capacitance*, and a *pseudo-inductance*. Because the phase differences introduced by these physical quantities are different, and depend on their arrangement, i.e., in *series* or in *parallel*, we must analyse separately these two possibilities.

Consequently, to propose criteria of classifying the drugs, we have considered other two electric schemes of the measuring cells, because the drug D, introduced in the electrolytic solution of the (RRD) *dielectrode*, changes the figure1, either in figure1*, corresponding to a *multielectrode* $(ME)_D^*$, or in figure1**, corresponding to a *multielectrode* $(ME)_D^{**}$:

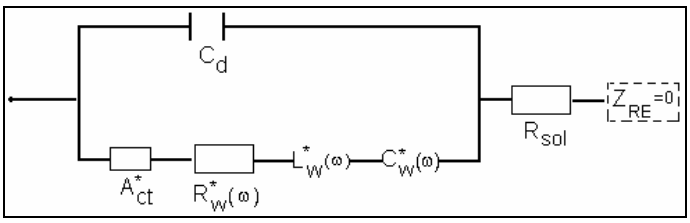


Figure 1*. The electric scheme of the measuring cell nedeed to obtain the Nyquist plot of the $(ME)_D^*$ multielectrode

respective:

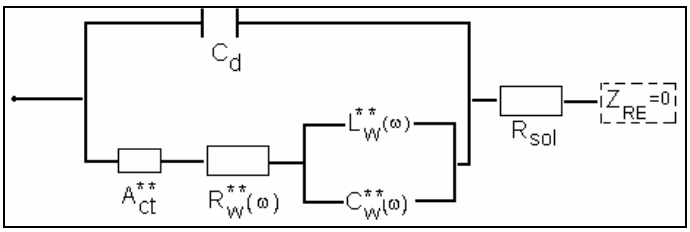


Figure 1.** The electric scheme of the measuring cell nedeed to obtain the Nyquist plot of the $(ME)_D^{**}$ mutielectrode.

Because KCl is in excess, the double layer capacity C_d and the solution resistance R_{sol}, maintain their values in all these schemes. Of course, a drug that *has no effect*, doesn't change the figure 1. Therefore, there are three classes of drugs, corresponding to these three electric schemes: (1), (1*) and (1**). To estimate the effects of drugs, we have decide to establish first the equations expressing in what conditions the electric schemes (1*), respective (1**), come back to the scheme (1), i.e., the effects of the respective drugs are *theoretically annihilated.*

Equations expressing the coming back of the figure(1*) to the figure(1)

As one knows, in the complex plane, the impedance of an inductance L is $\omega L\, j$, and of a capacitance C is $-\frac{1}{\omega C}\, j$. Then, the impedance of the

series arrangement Z^*_{series} must be equal to the impedance of the *Warburg pseudo-capacitance* $C_W(\omega)$, i.e.,

$$Z^*_{series}(\omega) = Z_{C_W}(\omega) \tag{5}$$

which, explicitly, writes:

$$\left(\omega L^*_W(\omega) - \frac{1}{\omega C^*_W(\omega)}\right) j = -\frac{1}{\omega C_W(\omega)}\, j \tag{6}$$

Eq.(6) represents the *first equation*, and expresses the equality between the values on the imaginary axes of the complex plane. From eq.(6) results:

$$\omega L^*_W(\omega) = \frac{1}{\omega C^*_W(\omega)} - \frac{1}{\omega C_W(\omega)} \tag{6'}$$

Because $\omega L^*_W(\omega)$ is a positive quantity, it follows:

$$C^*_W(\omega) = \alpha^*_D(\omega) C_W(\omega); \qquad \omega L^*_W(\omega) = \frac{1-\alpha^*_D(\omega)}{\alpha^*_D(\omega)} \cdot \frac{1}{\omega C_W(\omega)};$$
$$\alpha^*_D(\omega) < 1 \tag{7}$$

Eqs.(7) represent the consequences of eq.(6), and give the relations that must exist between *the theoretical quantities* $C^*_W(\omega)$, respective $L^*_W(\omega)$, and the *Warburg pseudo-capacitance* $C_W(\omega)$. As one sees, there are an infinity of possibilities, because there are an infinity of values $\alpha^*_D(\omega)$ less than unity.

Coming back to eq.(3), one sees that the product $R_W(\omega) C_W(\omega)$ depends only on the *radial frequency* ω. Consequently, *a second equation* will be the equality:

$$R^*_W(\omega) C^*_W(\omega) = R_W(\omega) C_W(\omega) \tag{8}$$

Taking into account the first equation(7), it results:

$$R_W(\omega) = \alpha^*_D(\omega) R^*_W(\omega); \qquad \alpha^*_D(\omega) < 1 \tag{9}$$

i.e., there are again an infinity of possibilities (because of $\alpha_D^*(\omega) \langle 1$) relating the *Warburg diffusion resistances* of the two electric schemes (1) and (1*).

The *third equation* gives the equality of the *total ohmical resistances* in the two schemes (i.e., of the values on the real axes the complex plane):

$$A_{ct}^* + R_W^*(\omega) = A_{ct} + R_W(\omega) \tag{10}$$

Using eq.(9), results:

$$\boxed{R_{sol} + A_{ct} = [1-\alpha_D^*(\omega)]\, R_W^*(\omega) + R_{sol} + A_{ct}^*} \tag{11}$$

if one introduce the solution resistance too.

Equations expressing the coming back of the figure(1**) to the figure(1)

Now the impedance of the parallel arrangement $Z_{parallel}^{**}$ must be equal to the impedance of the *Warburg pseudo-capacitance* $C_W(\omega)$:

$$Z_{parallel}^{**}(\omega) = Z_{C_W}(\omega), \text{ i.e., } \quad 1/\, Z_{parallel}^{**}(\omega) = 1/\, Z_{C_W}(\omega) \tag{12}$$

which, explicity, writes:

$$\frac{1}{\omega L_W^{**}(\omega)\, j} + \omega C_W^{**}(\omega)\, j = \omega C_W(\omega)\, j \tag{13}$$

Eq.(13) represents the *first equation*, and expresses the equality between the values on the imaginary axes of the complex plane. From eq.(13) results:

$$1/\, \omega L_W^{**}(\omega) = \omega C_W^{**}(\omega) - \omega C_W(\omega) \tag{13'}$$

$1/\, \omega L_W^{**}(\omega)$ being a positive quantity, it follows:

$$\boxed{\begin{array}{l} C_W^{**}(\omega) = \dfrac{1}{\alpha_D^{**}(\omega)} C_W(\omega); \qquad \omega L_W^{**}(\omega) = \dfrac{\alpha_D^{**}(\omega)}{1-\alpha_D^{**}(\omega)} \cdot \dfrac{1}{\omega C_W(\omega)}; \\ \alpha_D^{**}(\omega) \langle 1 \end{array}} \tag{14}$$

Eqs.(14) give the relations that must exist between the *theoretical quantities* $C_W^{**}(\omega)$, respective $L_W^{**}(\omega)$, and the *Warburg pseudo-capacitance* $C_W(\omega)$.

The *second equation* is similar to eq.(8), i.e.,

$$R_W^{**}(\omega)\, C_W^{**}(\omega) = R_W(\omega)\, C_W(\omega) \tag{15}$$

and taking into account the first equation(14), results:

$$\boxed{R_W(\omega) = \frac{1}{\alpha_D^{**}(\omega)} \cdot R_W^{**}(\omega); \qquad \alpha_D^{**}(\omega) \langle 1} \tag{16}$$

The *third equation* gives the equality of the *total ohmical resistances* in the two schemes (i.e., of the values on the real axes of the complex plane):

$$A_{ct}^{**} + R_W^{**}(\omega) = A_{ct} + R_W(\omega) \tag{17}$$

which, using eq.(16), writes:

$$\boxed{R_{sol} + A_{ct} = \left[1 - \frac{1}{\alpha_D^{**}(\omega)}\right] R_W^{**}(\omega) + R_{sol} + A_{ct}^{**}} \tag{18}$$

if one introduces the solution resistance too.

Finally, from eqs.(7, 9 and 11) one sees that for $\alpha_D^{*} < 1$, the *pseudo-inductance* $L_W^{*}(\omega)$ is different of zero, and $C_W^{*}(\omega)$, $R_W^{*}(\omega)$ and A_{ct}^{*} are different of $C_W(\omega)$, $R_W(\omega)$ and A_{ct}. In other words, for $\alpha_D^{*}(\omega) < 1$, the drug D belongs to the class (1^{*}). The same equations show that for $\alpha_D^{*}(\omega)=1$, $L_W^{*}(\omega)=0$, and $C_W^{*}(\omega)$, $R_W^{*}(\omega)$ and A_{ct}^{*} are equal to $C_W(\omega)$, $R_W(\omega)$ and A_{ct}. This means that for $\alpha_D^{*}(\omega)=1$, the drug D *has no effect*, i.e., belongs to the class(1). Similarly, eqs.(14, 16 and 18) show that for $\alpha_D^{**}(\omega) < 1$, the drug D belongs to the class (1^{**}), and for $\alpha_D^{**}(\omega)=1$, the drug D *has no effect*, i.e., belongs to the class (1). Generally, $\alpha_D^{*}(\omega) \neq \alpha_D^{**}(\omega)$,because there are an infinity of drugs belonging to the class(1^{*}), as well as an infinity of drugs belonging to the class(1^{**}). Unfortunately, the use of the pair $\alpha_D^{*}(\omega)$, $\alpha_D^{**}(\omega)$, *as a criterion of classifying the drugs*, has an important disadvantage, namely, the fact that their values are both less than unity, i.e., they are *on the same side of the unity*. It is necessary to find a pair of quantities, one for the class(1^{*}), the other for the class(1^{**}), whose values are *on the left, respective right, side of a reference value.*

The Thomson radial frequency $\omega_{Th,s}=\left[L_W^*(\omega)\,C_W^*(\omega)\right]^{-\frac{1}{2}}$ of the series circuit considered instead of Warburg pseudo-capacitance $C_W(\omega)$

From eqs.(7), one gets:

$$\omega_{Th,s}=\left[L_W^*(\omega)\,C_W^*(\omega)\right]^{-\frac{1}{2}}=\left[\frac{1-\alpha_D^*(\omega)}{\omega^2}\right]^{-\frac{1}{2}}=\frac{\omega}{\sqrt{1-\alpha_D^*(\omega)}} \quad (19)$$

which, for $\omega=\omega_1$, i.e., the smallest radial frequency used (say 0.2Hz = 1.256s^{-1}), becomes:

$$\omega_{Th,s}\left[\alpha_D^*(\omega_1)\right]=\frac{\omega_1}{\sqrt{1-\alpha_D^*(\omega_1)}} \quad (19')$$

Eq.(19') shows that for $\alpha_D^*(\omega_1)=0$, the *Thomson radial frequency* is equal to ω_1, i.e., ω_1 represents the *resonance Thomson radial frequency* of the series circuit ⟵$L_W^*(\omega)$—$C_W^*(\omega)$⟶ of the scheme (I*). Because $0\le\alpha_D^*(\omega_1)\langle 1$, it folows that:

$$\omega_1\le\omega_{Th,s}[0\le\alpha_D^*(\omega_1)\langle 1]\langle\infty \quad (20)$$

i.e., the values of the *Thomson radial frequencies* $\omega_{Th,s}[\alpha_D^*(\omega_1)]$ are greater than the *resonance Thomson radial frequency* $\omega_{Th,s}[\alpha_D^*(\omega_1)=0]=\omega_1$, i.e., on the real axes, they are situated on the right hand side of the *reference value* ω_1.

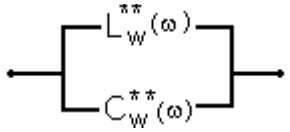
The Thomson radial frequency $\omega_{Th,s}=\left[L_W^{**}(\omega)\,C_W^{**}(\omega)\right]^{-\frac{1}{2}}$ of the parallel circuit considered instead of the Warburg pseudo-capacitance $C_W(\omega)$

From eqs.(14) one gets:

$$\omega_{Th,p}=[L_W^{**}(\omega)\,C_W^{**}(\omega)]^{-\frac{1}{2}}=\left[\frac{1}{\omega^2\left[1-\alpha_D^{**}(\omega)\right]}\right]^{-\frac{1}{2}}=\omega\sqrt{1-\alpha_D^{**}(\omega)} \quad (21)$$

which, for $\omega=\omega_1$, becomes:

$$\omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right]=\omega_1\sqrt{1-\alpha_D^{**}(\omega_1)} \quad (21')$$

Eq.(21') shows that for $\alpha_D^{**}(\omega_1)=0$, ω_1 represence also the *resonance Thomson radial frequency* of the parallel circuit  of the scheme (I**). Because $0 \le \alpha_D^{**}(\omega_1) \le 1$, it follows that:

$$\omega_1 \ge \omega_{Th,p}[\alpha_D^{**}(\omega_1)] \ge 0 \tag{22}$$

i.e, the values of the *Thomson radial frequencies* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ are less than the *resonance Thomson radial frequency* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)=0]=\omega_1$, i.e., on the real axes, they are situated on the left hand side of the *reference value* ω_1.

From the inequalities (15 and 17), results that *the pair* $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$, $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ *satisfies the necessary conditions for being used as criterion of classifying the drugs.*

Indeed, for a drug belonging to the class(1), i.e, *having no effect*, because both $\alpha_D^{*}(\omega_1)$ and $\alpha_D^{**}(\omega_1)$, tend to unity, the *Thomson radial frequency* $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ will tend to infinity, while the *Thomson radical frequency* $\omega_{Th,p}[\alpha_P^{**}(\omega_1)]$ will tend to zero. For the drugs belonging to the class (1*), the classifying criterion will be the *Thomson radial frequency* $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$, while for the drugs belonging to the class(1**), the classifying criterion will be the *Thomson radial frequency* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$.

From a series of drugs belonging to the class(1*), the most efficient is that corresponding to the smallest value $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$. From a series of drugs belonging to the class (1**), the most efficient is that corresponding to the greatest value $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$.

The expression of $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ in terms of A_{ct}, A_{ct}^{*} and $R_W^{*}(\omega_1)$

From eq.(11) results:

$$1-\alpha_D^{*}(\omega_1)=\frac{R_{sol}+A_{ct}-\left(R_{sol}+A_{ct}^{*}\right)}{R_W^{*}(\omega_1)} \tag{23}$$

To go further, we remind that the parametric equation giving the real part of a Nyquist plot in the domain of very small frequencies (round $\upsilon = \omega/2\pi = 0.2$Hz), is (see[22, 23]):

$$\mathrm{Re}(\omega) \cong R_{sol} + A_{ct} + \frac{J}{\sqrt{2\pi}} B_d\, \omega^{-1/2} = R_{sol} + A_{ct} + \frac{B_d}{2\omega^{1/2}} \quad (24)$$

where J represents the Fresnel integral:

$$J = \int_0^{\infty} \frac{\cos x}{x^{1/2}} dx = \sqrt{\frac{\pi}{2}} \quad (24')$$

The last term on the right hand side of eq.(24), represents the *Warburg diffusive* resistance $R_W(\omega)$, and thus (for $\omega_1 = 1.256 s^{-1}$):

$$1 - \alpha_D^*(\omega_1) = \frac{R_{sol} + A_{ct} - \left(R_{sol} + A_{ct}^*\right)}{0.446\, B_d^*} \quad (25)$$

Introducing the expression of $1 - \alpha_D^*(\omega_1)$ in eq.(19'), one gets:

$$\omega_{Th,s}\left[\alpha_D^*(\omega_1)\right] = \left[\frac{R_{sol} + A_{ct} - \left(R_{sol} + A_{ct}^*\right)}{0.446\, B_d^*}\right]^{-1/2} \omega_1 \quad (26)$$

(R_{sol} is maintained in eqs. (23-26), because we shall give equations for determining the sum of the solution and charge transfer resistances).

The expression of $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ in terms of A_{ct}, A_{ct}^{**} and $R_W^{**}(\omega_1)$

From eq.(18) results:

$$\left[1 - \frac{1}{\alpha_D^{**}(\omega_1)}\right] = \frac{R_{sol} + A_{ct} - \left(R_{sol} + A_{ct}^{**}\right)}{R^{**}(\omega_1)} \quad (27)$$

and explicitating the *Warburg diffusion resistance* $R^{**}(\omega_1)$ (see eqs. (24, 24')):

$$\left[1 - \frac{1}{\alpha_D^{**}(\omega_1)}\right] = \frac{R_{sol} + A_{ct} - \left(R_{sol} + A_{ct}^{**}\right)}{0.446\, B_d^{**}} \quad (27')$$

Further, after some trivial operations, eqs. (27' and 21') lead to:

$$\omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right] = \left\{\frac{R_{sol} + A_{ct}^{**} - (R_{sol} + A_{ct})}{0.446\, B_d^{**} - \left[R_{sol} + A_{ct} - \left(R_{sol} + A_{ct}^{**}\right)\right]}\right\}^{1/2} \omega_1 \quad (28)$$

Estimation of $R_{sol} + A_{ct}$ and B_d, in terms of the abscissae, $Re(\omega_1)$ and $Re(\omega_2)$, of the Nyquist plot of the RRD dielectrode; $\omega_1 = 1.256 s^{-1}$, $\omega_2 = 1.582 s^{-1}$

In figure 2, is given the shape of a Nyquist plot obtained by points, e.g., 10 points per decade (i.e., corresponding to a unitary distance on the logaritmic scale).

From eq.(24), it follows:

$$\frac{\mathrm{Re}(P_1) - X}{\mathrm{Re}(P_2) - X} \cong \left(\frac{\omega_1}{\omega_2}\right)^{-1/2}; \qquad X = R_{sol} + A_{ct} \tag{29}$$

i.e.,

$$R_{sol} + A_{ct} \cong \left[\mathrm{Re}(\omega_2) - \frac{\mathrm{Re}(\omega_1) - \mathrm{Re}(\omega_2)}{0.122}\right] \tag{30}$$

where:

$$\left(\frac{\omega_1}{\omega_2}\right)^{-1/2} - 1 = 0.122 \tag{30'}$$

Further, from eq.(24) written for ω_1, results:

$$B_d = 20.6\left[\mathrm{Re}(\omega_1) - \mathrm{Re}(\omega_2)\right] \tag{31}$$

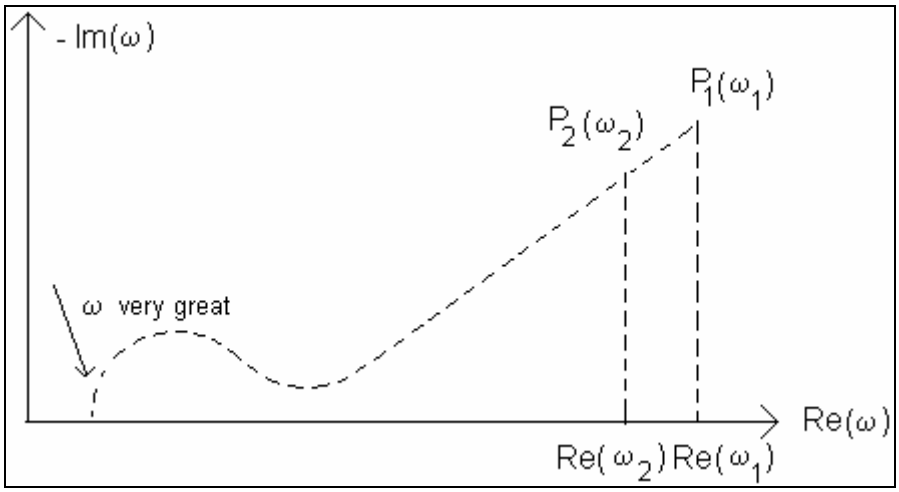


Figure 2. The shape of a Nyquist plot obtained by 10 points per decade. The first point corresponds to $\omega_1 = 1{,}256 s^{-1}$, and the second point to $\omega_2 = \omega_1 \cdot 10^{0.1} = 1.582 s^{-1}$.

Estimation of $R_{sol} + A_{ct}^{*}$ and B_d^{*}, in terms of the abscissae, $\mathrm{Re}^{*}(\omega_1)$ and $\mathrm{Re}^{*}(\omega_2)$ of the Nyquist plot of the $(ME)_D^{*}$ multielectrode; $\omega_1 = 1.256 s^{-1}$, $\omega_2 = 1.582 s^{-1}$

In this case, the Nyquist plot gives the dependence $-\mathrm{Im}^{*}(\omega)$ vs $\mathrm{Re}^{*}(\omega)$.

In rest, the procedure of getting the expressions of $R_{sol} + A_{ct}^{*}$ and B_d^{*} is the same(see eqs.(29-31)).

Thus:

$$R_{sol} + A_{ct}^{*} \cong \left[\mathrm{Re}^{*}(\omega_2) - \frac{\mathrm{Re}^{*}(\omega_1) - \mathrm{Re}^{*}(\omega_2)}{0.122} \right] \tag{32}$$

and:

$$B_d^{*} \cong 20.6[\mathrm{Re}^{*}(\omega_1) - \mathrm{Re}^{*}(\omega_2)] \tag{33}$$

Estimation of $R_{sol} + A_{ct}^{**}$ and B_d^{**} in terms of the abscissae, $\mathrm{Re}^{**}(\omega_1)$ and $\mathrm{Re}^{**}(\omega_2)$ of the Nyquist plot of the $(ME)_D^{**}$ multielectrode; $\omega_1 = 1.256 s^{-1}$, $\omega_2 = 1.582 s^{-1}$

In this case, the Nyquist plot gives the dependence $-\mathrm{Im}^{**}(\omega)$ vs. $\mathrm{Re}^{**}(\omega)$, and by applying the same procedure, one gets:

$$R_{sol} + A_{ct}^{**} \cong \left[\mathrm{Re}^{**}(\omega_2) - \frac{\mathrm{Re}^{**}(\omega_1) - \mathrm{Re}^{**}(\omega_2)}{0.122} \right] \tag{34}$$

respective:

$$B_d^{**} \cong 20.6\,[\mathrm{Re}^{**}(\omega_1) - \mathrm{Re}^{**}(\omega_2)] \tag{35}$$

The values $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ may be obtained by using the experimental values $\mathrm{Re}(\omega_1)$, $\mathrm{Re}(\omega_2)$ and $\mathrm{Re}^{*}(\omega_1)$, $\mathrm{Re}^{*}(\omega_2)$

Coming back to eq.(26), and using eqs.(30, 32, 33) one gets:

$$\omega_{Th,s}\left[\alpha_D^{*}(\omega_1)\right] \cong \left\{ \frac{1.121\left[\mathrm{Re}^{*}(\omega_1) - \mathrm{Re}^{*}(\omega_2)\right]}{a^{*} - b^{*}} \right\}^{1/2} \omega_1 \tag{36}$$

where

$$a^{*} = 1.122\,[\mathrm{Re}(\omega_1) - \mathrm{Re}^{*}(\omega_2)] \tag{36'}$$

and

$$b^{*} = \mathrm{Re}(\omega_1) - \mathrm{Re}^{*}(\omega_1) \qquad (36'')$$

Because of the inequalities (20), *the criterion* $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ *may be used to classify the drugs belonging to the class(1*), characterized by the inequality* $a^{*} \rangle\ b^{*}$*, or to show that a drug has no effect, i.e., belongs to the class(1), characterized by the equality* $a^{*} \cong b^{*}$ *when* $\omega_{Th,s}[\alpha_D^{*}(\omega_1)] \to \infty$.

The values $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ **may be obtained by using the experimental values** $\mathrm{Re}(\omega_1)$**,** $\mathrm{Re}(\omega_2)$ **and** $\mathrm{Re}^{**}(\omega_1)$**,** $\mathrm{Re}^{**}(\omega_2)$

Coming back to eq.(28), and using eqs.(30, 34, 35), one gets:

$$\omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right] \cong \left\{\frac{-a^{**} + b^{**}}{1.121\left[\mathrm{Re}^{**}(\omega_1) - \mathrm{Re}^{*}(\omega_2)\right] - a^{**} + b^{**}}\right\}^{1/2} \omega_1 \qquad (37)$$

where:

$$a^{**} = 1.122\ [\mathrm{Re}(\omega_2) - \mathrm{Re}^{**}(\omega_2)] \qquad (37')$$

and:

$$b^{**} \cong \mathrm{Re}(\omega_1) - \mathrm{Re}^{**}(\omega_1) \qquad (37'')$$

Because of the inequalities(22), *the criterion* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ *may be used to classify the drugs belonging to the class(1**), characterized by the inequality* $a^{**} \langle\ b^{**}$*, or to show that a drug has no effect, i.e., belongs to the class(1), characterized by the equality* $\alpha^{**} \cong b^{**}$*, when* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)] \to 0$.

The necessary steps in applying the procedure of classifying and testing the efficiency of drugs.

1. One records the Nyquist plot of the RRD dielectrode, and one gets the values Re(ω_1) and Re(ω_2).

2. One records the Nyquist plot of the multielectrode = RRD containing the investigated drug D, and one gets the values corresponding to the abscissae of the first two points $P_1(\omega_1)$, $P_2(\omega_2)$. These values may be, either $\mathrm{Re}^{*}(\omega_1)$, $\mathrm{Re}^{*}(\omega_2)$, or $\mathrm{Re}^{**}(\omega_1)$, $\mathrm{Re}^{**}(\omega_2)$, depending on the type of the multielectrode, i.e., $(ME)_D^{*}$ or $(ME)_D^{**}$.

One decides by means of the inequalities $a^{*} \rangle b^{*}$ or $a^{**} \langle\ b^{**}$.

3. If $a^* \rangle b^*$ one concludes that *D belongs to the class (1*), and* $(ME)_D = (ME)_D^*$

4. If $a^{**} \langle b^{**}$, one concludes that *D belongs to the class (1**), and (ME) = (ME**)*$_D$

5. If $a^* \cong b^*$ (when also $a^{**} \cong b^{**}$), one concludes that *D has no effect, i.e., belongs* to the class(1), and (ME)= RRD.

6. If D∈ (1*), one obtains the *radial Thomson frequency* $\omega_{Th,s}[\alpha_D^*(\omega_1)]$, by applying equation(36).

7. If D∈ (1**), one obtains the *radial Thomson frequency* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$, by applying equation(37).

In conclusion, for getting the values $\omega_{Th,s}[\alpha_D^*(\omega_1)]$, respective $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ sufice to take, from the corresponding Nyquist Plots, only two values, $\mathrm{Re}[P_1(\omega_1)]$ and $\mathrm{Re}[P_2(\omega_2)]$, and to apply the formulae (36) and (37).

EXPERIMENTAL SECTION

Method of recording the Nyquist plots

As we have already said(see the end of the INTRODUCTION chapiter) the figure(1) of the (RRD)- dielectrode has proved to be adequate for explaining the Nyquist plots in the domain of very small values of ω. In other words, to explain the phase difference between the current and the tension, suffice to use *one single theoretical quantity*, i.e., the *Warburg pseudo-capacitance* $C_W(\omega)$.

In this paper, one analyzes the effect that some drugs have upon the electrochemical properties of the reference redox dielectrode(RRD). These drugs have been introduced in the electrolytic solution of the *reference redox dielectrode*, maintaining the total volume of the solution at V=300ml. In this way, the electrochemical system(eq.(1)) of the *reference redox dielectrode*(1) transforms in the electrochemical systems of the *redox multielectrodes*: $(ME)_D^*$, or $(ME)_D^{**}$, i.e., of:

Pt | $[Fe(CN)_6]^{3-}$ / $[Fe(CN)_6]^{4-}$, KCl(in excess), v ml drug D$\in$(1*),
O_2 physically dissolved (38)

or:

Pt | $[Fe(CN)_6]^{3-}$ /$[Fe(CN)_6]^{4-}$, KCl(in excess), v ml drug D$\in$(1**),
O_2 physically dissolved (38')

depending on the type of schemes: (1*) or (1**), of the measuring cells nedeed to obtain the Nyquist plots of the respective multielectrodes $(ME)_D^*$ or $(ME)_D^{**}$. The concentrations of all species, *excepting those of the investigated drugs*, are given with respect to the same total volume V= (V-v)+v = 300ml, and are equal in the three systems: (1), (38) and (38'). Because of this request, one may consider that the drugs that *don't have therapeutic effects*, *maintain the type of scheme(1) for the measuring cell nedeed to obtain their Nyquist plots*, i.e., that they belong to the class(1).

To perform the experiments a SP-150 Potentiostat/ Galvanostat Bio-Logic Science Instruments has been used.

The experiments have been made at equilibrium, i.e., at a *constant overtension* η =0V, and for each drug, four Nyquist plots have been recorded, using an amplitude of 10mV for the alternating overtension $\tilde{\eta}$, and radial frequencies between ω_1 =1.256s^{-1} and ω_N= 6.28x$10^5 s^{-1}$.

The Nyquist plots have been recorded by points, using 10 points per decade(i.e., for passing from a value ω' to the value ω'' =10ω'). For this reason, $\omega_2 = \omega_1 \cdot 10^{0.1}$=1.582$s^{-1}$.

Method of classifying the drugs

In Tables 1 and 2 one gives the method used for establishing to what class belongs the investigated drug.

Table 1. Method of establishing to what class of drugs belong the investigated drugs

Dielectrode	Re(ω_1) (Ω)	Re(ω_2) (Ω)	
RRD V= 300 ml	319 322 318 320	291 291 289 290	

Multielectrode	$\mathrm{Re}^{*}(\omega_1)$ or $\mathrm{Re}^{**}(\omega_1)$ (Ω)	$\mathrm{Re}^{*}(\omega_2)$ or $\mathrm{Re}^{**}(\omega_2)$ (Ω)	a^{*} or a^{**} (Ω)	b^{*} or b^{**} (Ω)	Conclusions
$(ME)_B$ V= 300ml v= 20ml	10447 10936 11688 12721	9944 10409 11125 12206	-10830 -10761 -12158 -13370	-10128 -10614 -11370 -12401	$a^{**} < b^{**}$ $B \in (I^{**})$ $(ME)_B = (ME)_B^{**}$
$(ME)_{Am}$ V= 300ml v= 30ml	3333 3032 3032 3168	2924 2871 2871 3010	-2954 -2895 -2897 -3052 -2950	-3014 -2710 -2714 -2848 -2822	$a^{**} < b^{**}$ $Am \in (I^{**})$ $(ME)_{Am} = (ME)_{Am}^{**}$
$(ME)_{Cf}$ V= 300ml v= 20ml	7622 6388 7465 9013	7391 6209 7256 8709	-7966 -6640 -7817 -9446	-7303 -6066 -7147 -8693	$a^{**} < b^{**}$ $Cf \in (I^{**})$ $(ME)_{Cf} = (ME)_{Cf}^{**}$
$(ME)_{Cf}$ V= 300ml v= 30ml	18773 21816 21443 22051	17761 20100 20235 21410	-19601 -22226 -22379 -23697	-18454 -21494 -21125 -21731	$a^{**} < b^{**}$ $Cf \in (I^{**})$ $(ME)_{Cf} = (ME)_{Cf}^{**}$

In these Tables:

B= Sweedish Bitter (Original Schweden Tropfen, BANO)
Am= Achillea Millefolium (S C Dacia Plant SRL Romania Sebes-Tincture)
Cf= Calendula flos (S C Hofigal S.A. Romania, Bucuresti- Tincture)
Uh= Urticae herba (S C Hofigal SA Romnaia, Bucuresti- Tincture)

Table 2. Method of establishing to what class of drugs belong the investigated drugs

Dielectrode	$\mathrm{Re}(\omega_1)$ (Ω)	$\mathrm{Re}(\omega_2)$ (Ω)	
RRD V= 300 ml	319 322 318 320	291 291 289 290	

Multielectrode	$\mathrm{Re}^{*}(\omega_1)$ or $\mathrm{Re}^{**}(\omega_1)$ (Ω)	$\mathrm{Re}^{*}(\omega_2)$ or $\mathrm{Re}^{**}(\omega_2)$ (Ω)	a^{*} or a^{**} (Ω)	b^{*} or b^{**} (Ω)	Conclusions
$(ME)_{Uh}$ V= 300ml v= 20ml	4235 3987 3745 3551	4039 3816 3582 3367	-4205 -3955 -3695 -3452	-3916 -3665 -3427 -3231	$a^{**} < b^{**}$ $U_h \in (I^{**})$ $(ME)_{Uh} = (ME)^{**}_{Uh}$
$(ME)_{Uh}$ V= 300ml v= 30ml	10769 11098 11236 11600	10330 10636 10843 11133	-11264 -11607 -11842 -12166	-10450 -10776 -10915 -11280	$a^{**} < b^{**}$ $Uh \in (I^{**})$ $(ME)_{Uh} = (ME)^{**}_{Uh}$
$(ME)_{Uh+Am}$ V= 300ml v= (20+20)ml	3029 3008 3200 3735	2871 2848 3023 3551	-2895 -2869 -3068 -3659	-2710 -2686 -2882 -3415	$a^{**} < b^{**}$ $(Uh+Am) \in (I^{**})$ $(ME)_{Ud+Am} = (ME)^{**}_{Ud+Am}$
$(ME)_{B+Am+Cf+Uh}$ V= 300ml v = (10+10+ 10+10)ml	3007 3256 3487 3478	2859 3107 3339 3804	-2881 -3160 -3422 -3943	-2688 -2934 -3169 -3658	$a^{**} < b^{**}$ $B+Am+Cf+Uh \in (I^{**})$ $(ME)_{B+Am+Cf+Uh} =$ $(ME)^{**}_{B+Am+Cf+Uh}$

The values (a^{*} or a^{**}), respective (b^{*} or b^{**}) have led to the conclusions given in the last columns of these tables, and show that all drugs investigated belong to the class (I**). Concerning the drug Am, the first two values (i.e., -2954Ω, -3014Ω) satisfy the inequality $a^{*} > b^{*}$, but the mean values (-2950Ω, -2822Ω) *justify the conclusion given in the last column of Table1.*

Estimation of the Thomson radial frequencies

Once the values of a^{**} and b^{**} known, one may go further and estimate the *Thomson radial frequencies* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ by using eq.(37). The results are given in tables 3 and 4.

As one may observe, in the case of the drug Am, the first value of a^{**} (i.e., -2954Ω has been replaced by the mean value -2950Ω (see Table 1)), and similarly the first value of b^{**} (i.e., -3014Ω) has been replaced by the mean value -2822Ω.

Table 3. The Thomson radial frequencies $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ estimated by using equation (37)

Drug	$\mathrm{Re}^{**}(\omega_1)$ (Ω)	$\mathrm{Re}^{**}(\omega_2)$ (Ω)	a^{**} (Ω)	b^{**} (Ω)	$\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ (s^{-1})	$\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ (s^{-1}) **Mean values**
B	10447	9944	-10830	-10128	0.935	
V=300ml	10936	10409	-10761	-10614	0.561	
v=20ml	11688	11125	-12158	-11370	0.936	0.857
	12721	12206	-13370	-12401	0.994	
Am	3333	2924	-2950	-2822	0.587	
V=300ml	3032	2871	-2895	-2710	0.894	
v=20ml	3032	2871	-2897	-2714	0.891	0.823
	3168	3010	-3052	-2848	0.919	
Cf	7622	7391	-7966	-7303	1.065	
V=300ml	6388	6209	-6640	-6066	1.081	
v=20ml	7465	7256	-7817	-7147	1.081	1.067
	9013	8709	-9446	-8633	1.042	
Cf	18773	17761	-19601	-18454	0.891	
V=300ml	21816	20100	-22226	-21494	0.659	
v=30ml	21443	20235	-22379	-21125	0.871	0.874
	22051	21410	-23697	-21731	1.075	

Table 4. The Thomson radial frequencies $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ estimated by using equation (37)

Drug	$\mathrm{Re}^{**}(\omega_1)$ (Ω)	$\mathrm{Re}^{**}(\omega_2)$ (Ω)	a^{**} (Ω)	b^{**} (Ω)	$\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ (s^{-1})	$\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ (s^{-1}) **Mean values**
Uh	4235	4039	-4205	-3916	0.947	
	3987	3816	-3955	-3665	0.965	
V=300ml	3745	3582	-3695	-3427	0.969	0.949
v=20ml	3551	3367	-3452	-3231	0.913	
Uh	10769	10330	-11264	-10450	0.992	
	11098	10636	-11607	-10776	0.986	
V=300ml	11236	10843	-11842	-10915	1.034	1.002
v=30ml	11600	11133	-12166	-11280	0.996	
Uh+Am	3029	2871	-2895	-2710	0.898	
	3008	2848	-2869	-2686	0.893	
V=300ml	3200	3023	-3068	-2882	0.874	0.898
v=(20+20)ml	3735	3551	-3659	-3415	0.925	
B+Am+	3007	2859	-2881	-2688	0.921	
Cf+Uh	3256	3107	-3160	-2934	0.952	
	3487	3339	-3422	-3169	0.976	0.954
V=300ml	3978	3804	-3943	-3658	0.968	
v=(10+10+						
+10+10)ml						

As one sees from the mean values of the *Thomson radial frequencies*, the *increase* of the concentration of the drug Cf (by passing from v=20ml to v=30ml) leads to a *decrease* of $\omega_{Th,p}[\alpha^{**}_{Cf}(\omega_1)]$, from 1.067 s^{-1}, to 0.874 s^{-1}. This is not *the normal case*, because by *increasing* the concentration, the efficiency of the drug must *increase* too. Consequently, because $\omega_{Th,p}[\alpha^{**}_{Cf}(\omega_1)] = \sqrt{1-\alpha^{**}_{Cf}(\omega_1)}\cdot\omega_1$, its value must *increase* from zero (when $\alpha^{**}_{Cf}=1$) towards ω_1 (when α^{**}_{Cf} =0), and *not to decrease* from 1.067s^{-1} to 0.874s^{-1}.

The *normal case* is that of the drug Uh, because by *increasing* its concentration $\omega_{Th,p}[\alpha^{**}_{Ud}(\omega_1)]$ *increases too*, from 0.949s^{-1} to 1.002s^{-1}.

A way of interpreting the obtained Thomson radial frequencies

To explain these two possibilities, one exemplifyed by the drug Cf, the other by the drug Uh, let's write eq.(27') in the form:

$$1-\frac{1}{\alpha^{**}_{D}(\omega_1)}=\frac{A_{ct}-A^{**}_{ct}}{0.446\,B^{**}_{d}} \tag{27''}$$

Further, coming back to the first equation(4), one gets:

$$\frac{1}{A_{ct}}=2\frac{\left(A/A_{ct1}+A/A_{ct2}\right)}{2}\cdot\frac{1}{A}=2\left(\overline{A/A_{ct}}\right)\cdot\frac{1}{A} \tag{38}$$

and thus:

$$A_{ct}=\frac{1}{2\left(\overline{A/A_{ct}}\right)}\cdot A \tag{38'}$$

Similarly:

$$\frac{1}{A^{**}_{ct}}=p\,\frac{\left(A^{**}/A^{**}_{ct1}+.....+A^{**}/A^{**}_{ctp}\right)}{p}\cdot\frac{1}{A^{**}} \tag{39}$$

and therefore:

$$A^{**}_{ct}=\frac{1}{p\left(\overline{A^{**}/A^{**}_{ct}}\right)}\cdot A^{**} \tag{39'}$$

Of course, for $R^{**}_{W}(\omega_1)=0.446B^{**}_{d}$, the second eq.(4) holds too, and then:

$$\frac{1}{B_d^{**}} = p \cdot \frac{\left(A^{**} / B_{d1}^{**} + ... + A^{*} / B_{dp}^{**}\right)}{p} \cdot \frac{1}{A^{**}} \tag{40}$$

i.e.,

$$0.446\, B_d^{**} = 0.446 \cdot \frac{1}{p\left(\overline{A^{**} / B_d^{**}}\right)} \cdot A^{**}$$

Using eqs.(38', 39' and 40), eq.(27") gets the form:

$$1 - \frac{1}{\alpha_D^{**}(\omega_1)} = \frac{\left[1/2\left(\overline{A/A_{ct}}\right)\right]A - \left[1/p\left(\overline{A^{**}/A_{ct}^{**}}\right)\right]A^{**}}{0.446\left[1/p\left(\overline{A^{**}/B_d^{**}}\right)\right]A^{**}} \tag{41}$$

Some important conclusions come out from eqs.(27" and 41):

A) The drug D∈ (1**) *doesn't adsorb and doesn't influence the charge transfer.*

Then:

$$A^{**} = A \quad \text{and} \quad 2\left(\overline{A/A_{ct}}\right) = p\left(\overline{A^{**}/A_{ct}^{**}}\right) \tag{42}$$

and consequently:

$$\alpha_D^{**}(\omega_1) = 1, \text{ i.e., } \quad \omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right] = 0 \tag{42'}$$

which also means D∈ (1)

B) The drug D∈(1**) *doesn't adsorb, but influences the charge transfer*.

Them:

$$A^{**} = A \qquad \text{and} \qquad 2\left(\overline{A/A_{ct}}\right) \neq p\left(\overline{A^{**}/A_{ct}^{**}}\right) \tag{43}$$

The situation:

$$2\left(\overline{A/A_{ct}}\right) < p\left(A^{**}/A_{ct}^{**}\right) \tag{43'}$$

is impossible, because would lead to the conclusion $1 - \frac{1}{\alpha_D^{**}(\omega_1)} > 0$, i.e., $\alpha_D^{**}(\omega_1) > 1$ (see eq.(41)). Therefore, the correct conditions of the case B, are:

$$A^{**} = A \qquad \text{and} \qquad 2\left(\overline{A/A_{ct}}\right) \rangle\ p\left(\overline{A^{**}/A_{ct}^{**}}\right) \quad (44)$$

Suppose now that by *increasing* the concentration of the drug D, one passes from $1-\frac{1}{\alpha_D^{**}(\omega_1)} = -k_1$, to $1-\frac{1}{\alpha_D^{**}(\omega_1)} = -k_2$, and $k_2 > k_1$. Then $\omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right]$ will *increase* from $\sqrt{1-\frac{1}{1+k_1}}\cdot\omega_1$ to $\sqrt{1-\frac{1}{1+k_2}}\cdot\omega_1$. Of course, if $k_2 < k_1$, $\omega_{Th,p}\left[\alpha_D^{**}(\omega_1)\right]$ will *decrease* from $\sqrt{1-\frac{1}{1+k_1}}\cdot\omega_1$ to $\sqrt{1-\frac{1}{1+k_2}}\cdot\omega_1$. Therefore, if the conditions(44) hold true, *both situations are possible*.

C) The drug D∈(1**) *adsorbs and influences the charge transfer*.

Then:

$$A^{**} \langle A\ ; \qquad 2\left(\overline{A/A_{ct}}\right) \neq p\left(\overline{A^{**}/A_{ct}^{**}}\right) \quad (45)$$

and:

$$1-\frac{1}{\alpha_D^{**}(\omega_1)} = \frac{\left[1/2\left(\overline{A/A_{ct}}\right)\right]\left(A/A^{**}\right) - \left[1/p\left(\overline{A^{**}/A_{ct}^{**}}\right)\right]}{0.446\left[1/p\left(\overline{A^{**}/B_d^{**}}\right)\right]} \quad (46)$$

Now, the correct conditions are:

$$A^{**} \langle A \text{ and } \left[1/2\left(A/A_{ct}\right)\right]\left(A/A^{**}\right) \langle \left[1/p\left(\overline{A^{**}/A_{ct}^{**}}\right)\right] \quad (47)$$

and again, *both situations are possible*.

D) The drug D∈(1**) *adsorbs but doesn't influence the charge transfer*.

Because $A/A^{**} \rangle 0$, and $2\left(\overline{A/A_{ct}}\right) = p\left(\overline{A^{**}/A_{ct}^{**}}\right)$ from eq.(46) results: $1-\frac{1}{\alpha_D^{**}(\omega_1)} \rangle 0$, which is *impossible*. Thus, *the case D, is not possible*.

This is a correct conclusion, because if there is adsorption, the exchange current densities of the electrode reactions must change their values.

Let's go further, and let's compare two different drugs, D_i and D_j, and let's suppose that these drugs satisfy the *conditions* of the case C), i.e.,

$$\left[1/2\left(\overline{A/A_{ct}}\right)\right]\left(A/{}_iA^{**}\right) \langle \ \left[1/p_i\left({}_iA^{**}/{}_iA_{ct}^{**}\right)\right] \tag{48}$$

$$\left[1/2\left(\overline{A/A_{ct}}\right)\right]\left(A/{}_jA^{**}\right) \langle \ \left[1/p_j\left({}_jA^{**}/{}_jA_{ct}^{**}\right)\right] \tag{48'}$$

respective:

$$1-\frac{1}{\alpha_{D_i}^{**}(\omega_1)} = \frac{\left[1/2\left(\overline{A/A_{ct}}\right)\right]\left(A/{}_iA^{**}\right)-\left[1/p_i\left(\overline{{}_iA^{**}/{}_iA_{ct}^{**}}\right)\right]}{0.446\left[1/p_i\left(\overline{{}_iA^{**}/{}_iB_d^{**}}\right)\right.} \tag{49}$$

$$1-\frac{1}{\alpha_{D_j}^{**}(\omega_1)} = \frac{\left[1/2\left(\overline{A/A_{ct}}\right)\right]\left(A/{}_jA^{**}\right)-\left[1/p_j\left(\overline{{}_jA^{**}/{}_jA_{ct}^{**}}\right)\right]}{0.446\left[1/p_j\left(\overline{{}_jA^{**}/{}_jB_d^{**}}\right)\right]} \tag{49'}$$

Then if the second member of eq.(49) is $-k_i$, the *Thomson radial frequencie* will be $\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] = \sqrt{1-\frac{1}{1+k_i}}\cdot\omega_1$. Similarly, if the second member of eq.(49') is $-k_j$, $\omega_{Th,p}[\alpha_{D_j}^{**}(\omega_1)]$ will be $\sqrt{1-\frac{1}{1+k_j}}\cdot\omega_1$. Depending on the values of k_i and k_j, *there are possible all three situations*, i.e.,

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \geq \omega_{Th,p}[\alpha_{D_j}^{**}(\omega_1)]$$

and:

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \langle \omega_{Th,p}[\alpha_{D_j}^{**}(\omega_1)]$$

Of course, it is possible to compare a drug D_i with a mixture of Drugs or even to compare two mixtures of drugs. To simplify the matter, we don't indicate the drugs which enter in the compositions of the respective mixtures. In our experiments we have used four drugs $D_i \in (1^{**})$, and two mixtures : M_1^{**} containing the drugs *Am* and *Uh*, and M_2^{**} containing all four drugs: B, Am, Cf and Uh (see Table 2). As for the numbers of electrode reactions in the multielectrodes containing the mixtures M_1^{**}, respective

M_2^{**}, we shall use the notations q_1, respective q_2. Finally, the quantities A^{**}, B_d^{**} in the presence of the mixtures M_1^{**}, respective M_2^{**}, will be denoted $\underline{1}A^{**}$, $\underline{1}B_d^{**}$, respective $\underline{2}A^{**}$, $\underline{2}B_d^{**}$. Thus, consider first, the comparison between $D_i \in (1^{**})$, and the mixture M_1^{**}. Then, eq.(49) remains valid, and instead of eq.(49'), appears:

$$1-\frac{1}{\alpha_{M_1}^{**}(\omega_1)}=\frac{[1/2(\overline{A/A_{ct}})](A/\underline{1}A^{**})-\left[1/q_1\left(\overline{\underline{1}A^{**}/\underline{1}A_{ct}^{**}}\right)\right]}{0.446\,[1/q_1(\overline{\underline{1}A^{**}/\underline{1}B_d^{**}})]} \quad (50)$$

In the case of the comparison between $D_i \in (1^{**})$ and the mixture M_2^{**}, eq.(49) remains still valid, and instead of eq.(50), appears:

$$1-\frac{1}{\alpha_{M_2}^{**}(\omega_1)}=\frac{[1/2(\overline{A/A_{ct}})](A/\underline{2}A^{**})-[1/q_2(\overline{\underline{2}A/\underline{2}A_{ct}^{**}})]}{0.446\,[1/q_2(\overline{\underline{2}A^{**}/\underline{2}B_d^{**}})]} \quad (50')$$

What it is important, is the fact that *in both comparisons*, *there are possible all three situation*, i.e.,

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \rangle \ \omega_{Th,p}[\alpha_{M_1}^{**}(\omega_1)$$

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \langle \ \omega_{Th,p}[\alpha_{M_1}^{**}(\omega_1)$$

respective:

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \rangle \ \omega_{Th,p}[\alpha_{M_2}^{**}(\omega_1)$$

$$\omega_{Th,p}[\alpha_{D_i}^{**}(\omega_1)] \langle \ \omega_{Th,p}[\alpha_{M_2}^{**}(\omega_1) \quad (51)$$

It is obvious that eqs.(50 and 50') describe the comparison between M_1^{**} and M_2^{**} with the same three possibilities, i.e.,:

$$\omega_{Th,p}[\alpha_{M_1}^{**}(\omega_1)] \geq \omega_{Th,p}[\alpha_{M_2}^{**}(\omega_1)]$$

$$\omega_{Th,p}[\alpha_{M_1}^{**}(\omega_1)] \langle \ \omega_{Th,p}[\alpha_{M_2}^{**}(\omega_1)] \quad (52)$$

CONCLUDING REMARCS

The mean values of the obtained *Thomson radial frequencies* (see Tables 3 and 4) are represented under the form of an *histogram* in Figure2. On the horizontal axis are the investigated drugs, and mixtures, put in the sequence given in Table 3 and 4, and the heights of the vertical segments give the mean values of the corresponding *Thomson radial frequencies* $\omega_{Th,p}[\alpha^{**}(\omega_1)]$. The drugs used in two different concentrations, are indicated by the index numbers 1 and 2.

Because $\omega_{Th,p}[\alpha^{**}(\omega_1)] = \omega_1 \sqrt{1-\alpha^{**}(\omega_1)}$ and $0 \le \alpha^{**} \le 1$, we have divided the class(I**) in four subclasses, which express the degree of efficiency of the investigated drugs and mixtures of drugs. Some important conclusions come out from this histogram:

- all the values $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ are less than the *resonance Thomson radial frequency* $\omega_{Th,p}[\alpha_D^{**}(\omega_1)=0] = \omega_1 = 1.256 s^{-1}$, showing that all drugs and mixtures investigated belong to the class(1**);

- the *resonance Thomson radial frequency* ω_1 corresponds to the *greatest efficiency* of a drug(or a mixture of drugs). Therefore, the efficiency *increases* if $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ *increases* towards ω_1.

- it is obvious that for drugs belonging to the class(1*), $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ are *greater* than the *resonance Thomson radial frequency*, which remains ω_1 too, and that their efficiency *increases* if $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ *decreases* towards ω_1. It is easy to verify, by means of equation $\omega_{Th,s}[\alpha_D^{*}(\omega_1)] = \omega_1 / \sqrt{1-\alpha_D^{*}(\omega_1)}$, that the four subclasses of the class(1*), corresponding to the values $\alpha_D^{*}(\omega_1)$ = 0; 0.25; 0.50; 0.75 and 1, will be given by the values $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ = (1.256; 1.450; 1.776; 2.512 and ∞) s^{-1}.

In this way, $\omega_{Th,s}[\alpha_D^{*}(\omega_1)]$ and $\omega_{Th,p}[\alpha_D^{**}(\omega_1)]$ represent *two criteria of classifying the drugs in eight subclasses*, namely four subclasses for each general class, i.e., (1*), respective (1**). Indeed, suffice to estimate how far away are the values of the respective *Thomson radial frequencies* from ω_1, i.e., from the *resonance Thomson radial frequency, which expresses the greatest efficiency.*

- finally, the values of the *Thomson radial frequencies* given in figure 3 prove the correctness of eqs.(49), (49') and (50), (50'), by which one may explain the effects of adsorption processes, and of the new charge transfer processes (see "*A way of interpreting the obtained Thomson radial frequencies*").

The great difference between the efficiencies of Cf_1 and Cf_2, indicates that the drug Cf has *an important adsorption*, while the drugs entering in the subclass of *good efficiency*: adsorb and also lead to new charge transfer reactions, or at least, influence the existente reactions. Our future work will try to analyse separately these two kinds of effects.

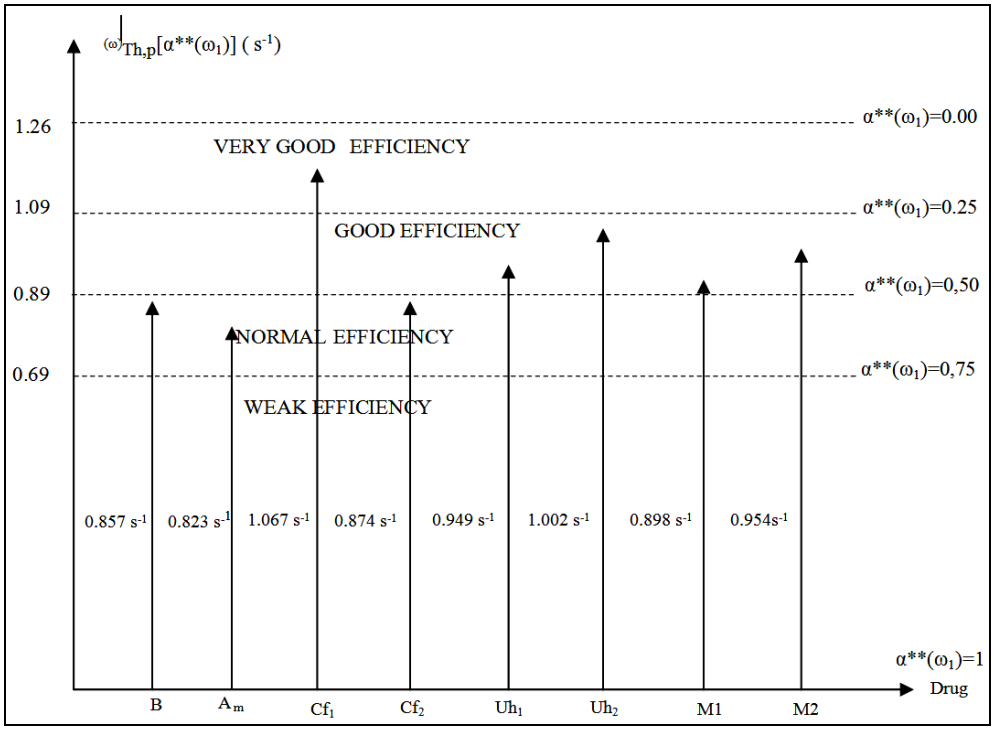


Figure 3. Histogram of the Thomson radial frequencies corresponding to the investigated drugs and mixtures of drugs

REFERENCES

1. N. Bonciocat, S. Borca and St. Moldovan, *Bulg. Acad. Sci. Commun*. *Depart. Chem*., **1990**, *23*, 289.
2. Adina Cotarta, Ph.D Thesis, Chemical Research Institute, Bucharest, **1992**.
3. N. Bonciocat, *Electrokhimiya*, **1993**, *29*, 97.
4. N. Bonciocat, *Electrochimie si Aplicatii*, Dacia Europa - Nova, Timisoara, **1996**, chapter 5, 262.
5. N. Bonciocat and A. Cotarta, *Revue Roumaine de Chimie*, **1998**, *43*, 925

6. N. Bonciocat and A. Cotarta, *Revue Roumaine de Chimie*, **1998**, *43*, 1027.
7. N. Bonciocat, "*Alternativa Fredholm in Electrochimie*", Editura MEDIAMIRA, Cluj-Napoca, **2005**, chapter 2.
8. N. Bonciocat, *Electrochimie si Aplicatii*, Dacia Europa-Nova, Timisoara, **1996**, chapter 6, 268-277.
9. N. Bonciocat, *Electrochimie si Aplicatii*, Dacia Europa-Nova, Timisoara, **1996**, chapter 6, 278.
10. Adina Radu(Cotarta), Ph.D. These, Institut National Polytechnique de Grenoble, **1997**.
11. N. Bonciocat and A. Cotarta, "A new approach based on the theory of variational calculus in studying the electrodeposition process of chromium in the system $Cr^0/CrCl_2$, LiCl-KCl", *Contract Copernicus 1177-2* "Utilisation de sels fondus en metallurgie", Final Report of European Community, July **1998**.
12. I.O. Marian, E. Papadopol, S. Borca and N. Bonciocat*, Studia Universitatis Babes-Bolyai, Cluj-Napoca, Ser. Chemia*, **1998**, *43*, 91.
13. N. Bonciocat, *Scientific Bulletin Chemistry Series Politechnica University Timisoara*, **1998**, *43*, 5.
14. N. Bonciocat, "*Alternativa Fredholm in Electrochimie*", Editura MEDIAMIRA, Cluj-Napoca, vol. I, **2005**, chapter 5.
15. N. Bonciocat, E. Papadopol, S. Borca and I.O. Marian, *Revue Roumaine de Chimie*, **2000**, *45*, 981.
16. N. Bonciocat, E.Papadopol, S. Borca and I.O. Marian, *Revue Roumaine de Chimie*, **2000**, *45*, 1057.
17. I.O. Marian, R. Sandulescu and N. Bonciocat, *Journal of Pharmaceutical and Biomedical Anal*ysis, **2000**, *23*, 227.
18. I.O. Marian, N. Bonciocat, R. Sandulescu and C. Filip, *Journal of Pharmaceutical and Biomedical Anal*ysis, **2001**, *24*, 1175.
19. N. Bonciocat, A. Cotarta, J. Bouteillon and J.C. Poignet, *Journal of High Temperature Material Processes*, **2002**, *6*, 283.
20. N. Bonciocat, I.O. Marian, R. Sandulescu, C. Filip and S. Lotrean, *Journal of Pharmaceutical and Biomedical Analysis*, **2003**, *32*, 1093.
21. N. Bonciocat, "*Alternativa Fredholm in Electrochimie*", Editura MEDIAMIRA, Cluj-Napoca, vol. II, **2006**, chapter 2, 25.
22. N. Bonciocat and A. Cotarta, *"Spectroscopia de Impedanta Electrochimica in cazul limitarilor de transfer de sarcina si difuziune",* Editura Printech, Bucuresti, **2005**.
23. N. Bonciocat and I.O. Marian, *" Metoda Impedantei Faraday si variantele sale"* Presa Universitara Clujeana, **2006**, chapter 5.
24. N. Bonciocat and A. Cotarta, *Annals of West University of Timisoara, Series Chemistry,* **2006**, *15*, 137.
25. N. Bonciocat and A. Cotarta, *Scientific Bulletin Chemistry Series Politehnica University Timisoara*, **2007**, *52*, 1-2, 90.
26. N. Bonciocat, *Studia Universitatis Babes-Bolyai, Cluj-Napoca, Seria Chemia*, **2008***,* LIII, 1, 31.
27. N. Bonciocat, A. Cotarta, *Scientific Bulletin Chemistry Series Politehnica University Timisoara,* **2009**, in press.