

Electrochemical Aspects of Treatment of Tissue with Direct Current

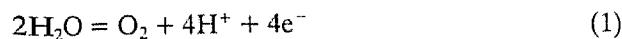
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INTRODUCTION

By using platinum electrodes in electrolysis in tissue, the main reactions are decomposition of water and oxidation or reduction of substances dissolved in the water. Consequently, at the anode this means evolution of oxygen in addition to acidification and formation of chlorine according to the following reactions:



For thermodynamic reasons oxygen should be formed at lower anode potentials than chlorine. However, by the different kinetics of these reactions, chlorine is formed more easily than oxygen and therefore the current yield for the formation of chlorine is relatively high and depends among other things on the anodic current density. Under optimal conditions, the current yield for the formation of chlorine will reach 50% at the most (10).

The decomposition of water at the anode results in pH values down to one in the tissue close to the anode (9). Secondary reactions of chlorine formed at the anode will have only negligible influence on pH. It is assumed that the chlorine is spread into the surrounding acidified tissue mainly by diffusion. The resulting rate of this spreading process is affected by the capacity of the tissue to bind chlorine chemically (10, 11). The bleaching effect of chlorine causes a light zone close to the anode.

The liberated hydrogen ions are spread in the surrounding tissue by migration and diffusion. The rate of this spreading process is affected among other things by the gradient of the electric field, the concentration gradient, the geometrical conditions and the buffer capacity of the surrounding tissue. Due to the formation of haematin, the acidified tissue becomes dark brown (7).

The toxic effects of hydrogen chloride and chlorine are documented in the literature (1, 5).

Calculations have been made for the two major anodic reactions. As a first approximation just one-dimensional diffusion is considered for the two interesting species, chlorine and hydrogen ion. For the hydrogen ion this means an under-estimation of its resulting spreading rate. To be able to include the

migration part more accurate experimental data and a more complex mathematical model are needed.

THE SPREADING OF CHLORINE IN THE TISSUE

The spreading of chlorine by diffusion is retarded by its reaction with the surrounding tissue. We may assume that chlorine reacts very rapidly and completely, so the spreading rate is controlled by the diffusion process (10). Furthermore, the fluid at the anode surface will be saturated with chlorine, while the free chlorine concentration is zero at the diffusion front. According to data in the literature the electrolytically treated tissue contains, in the dried state, about 6% (w/w) covalently bound chlorine (10). This corresponds approximately to 2% (w/w) *in vivo* in tissue neglecting drying effects caused by electro-osmosis. Since the saturation concentration of chlorine, $c_s(\text{Cl}_2)$, is well below that of the chlorine content covalently bound in the tissue, we may assume a uniform concentration gradient through the chlorinated layer in the tissue. By adopting these approximations this moving boundary problem may be solved analytically. Solutions to analogous problems can be found in the literature (3):

$$x(\text{Cl}_2) = \sqrt{\frac{2D(\text{Cl}_2)c_s(\text{Cl}_2)t}{W\rho}} \quad (3)$$

The following parameters are used here:

- $x(\text{Cl}_2)$ = distance from the surface of a plate anode to the reaction front in the tissue affected by chlorine
- $c_s(\text{Cl}_2)$ = saturation concentration of chlorine in tissue at 37°C (3×10^{-3} g/cm³) (6)
- $D(\text{Cl}_2)$ = estimated diffusion coefficient for chlorine in tissue at 37°C (4×10^{-5} cm²/sec) (2)
- W = content (w/w) of covalently bound chlorine in tissue (2%)
- ρ = estimated density of the tissue (g/cm³)
- t = time of electrolysis (sec)

Furthermore, we consider a current density of 20 mA/cm², while the current yield (η) for formation of chlorine is assumed to be 50%. Faraday's law is used

Table I. Calculated spreading of chlorine in tissue close to a plate anode of platinum after various times of electrolysis, and the degree of its utilisation

t (secs):	10	10 ²	6 × 10 ²	10 ³	2 × 10 ³	5 × 10 ³	8 × 10 ³	10 ⁴
x (mm):	0.11	0.35	0.85	1.10	1.55	2.45	3.10	3.46
ν (%):	—	—	98	76	54	35	27	24

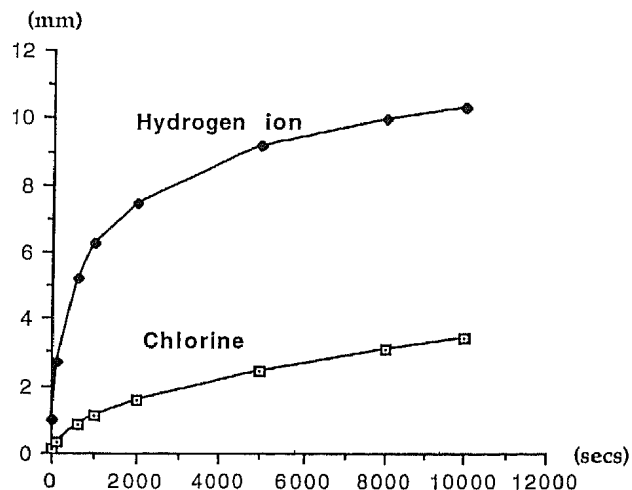


Fig. 1. The spreading of hydrogen ion and chlorine during electrolysis. x-axis: time of electrolysis (sec), y-axis: spreading distance (mm) for chlorine and hydrogen ion (pH 3), respectively.

for checking the degree of utilisation (ν) of the chlorine formed at the anode.

$$n(\text{Cl}_2) = \frac{it\eta}{zF} \quad (4)$$

where $n(\text{Cl}_2)$ = number of moles of chlorine
 i = anodic current density (2×10^{-2} A/cm²)
 t = time of electrolysis (sec)
 η = current yield (50%)
 z = valency change per mole chlorine formed at the anode ($z = 2$)
 F = Faraday's constant ($96,500$ As/mole⁻¹)

The results are given in Table I and they are also plotted in Fig. 1.

These results reveal that the diffusion rate of chlorine is slower at the beginning of the electrolysis process and the values for the spreading zone are too high, at times < approx. 600 seconds. After that, the solution close to the anode may be saturated by chlorine and in the continuation of this process there are losses of chlorine mainly by leakage from the anode zone out to the air.

THE SPREADING OF HYDROGEN IONS IN THE TISSUE

The spreading of hydrogen ions is limited by the

buffer capacity of the surrounding tissue. The buffer capacity is mainly maintained by the circulating blood, and on the basis of available literature data its total buffer capacity is estimated to be 80×10^{-3} (M) (12). We assume a steady state value of pH 1 close to the anode surface during the electrolysis at the current density adopted here (9). Hydrogen ions are then transported outwards both by diffusion and migration. However, as a first approximation we just consider the diffusion process for a minor species, since in the tissue we have a supporting electrolyte of NaCl with the bulk concentration 0.16 M. The spreading of hydrogen ions is counteracted by a flux of buffer substances emerging from the blood. In this case we assume that diffusion of the buffering species is the main transport process in a narrow reaction layer just beyond the front of the acidified zone.

On the basis of these assumptions we may express the current situation by the following equations and boundary conditions.

We try to adopt a solution of the form

$$\frac{c_{\text{H}^+}}{c_{\text{H}^+}^0} = a_1 + a_2 \operatorname{erf} \frac{x}{\sqrt{4D_{\text{H}^+}t}} \quad (5)$$

where

c_{H^+} = concentration of hydrogen ions (M);
 $c_{\text{H}^+}^0$ = concentration of hydrogen ions (M) at the anode surface;
 a_1 and a_2 are constants to be determined by the boundary conditions;
 x = distance perpendicular to the surface of the anode ($x = 0$ at the anode surface);
 D_{H^+} = polarographic diffusion coefficient for hydrogen ion (10^{-4} cm²/sec);
 t = time of electrolysis (secs);

$$\operatorname{erf} x = \frac{2}{\sqrt{\pi}} \int_0^x e^{-t^2} dt$$

Fick's second law is assumed to be valid for the diffusion of the hydrogen ions.

$$\frac{\partial c_{\text{H}^+}}{\partial t} = D_{\text{H}^+} \frac{\partial^2 c_{\text{H}^+}}{\partial x^2} \quad 0 < x \leq x'(t) \quad (6)$$

$x'(t)$ is the coordinate for the moving boundary where c_{H^+} is 10^{-7} M. For the assumed monovalent buffering species we have

$$j_{B-} = D_{B-} \left| \frac{\partial c_{B-}}{\partial x} \right| \quad (7)$$

where

j_{B-} = diffusion flow of buffering species (mole/cm², sec)

D_{B-} = mean diffusion coefficient for buffering species (10⁻⁵ cm²/sec)

$\left| \frac{\partial c_{B-}}{\partial x} \right|$ = concentration gradient for B⁻ ions

The concentration gradient for B⁻ ions is assumed to be constant during the electrolysis. By the previously made assumptions its value may be

$$\frac{80 \cdot 10^{-6}}{10^{-1}} = 8 \cdot 10^{-4} \text{ mole/cm}^4.$$

The thickness of the reaction layer is assumed to be 1 mm. At the fraction frontier we have

$$c_{H^+}(x', t) = 10^{-7} \text{ M} (\approx 0) \quad (8)$$

By total differentiation we obtain

$$dc_{H^+} = \left(\frac{\partial c_{H^+}}{\partial x'} \right)_t dx' + \left(\frac{\partial c_{H^+}}{\partial t} \right)_{x'} dt = 0 \quad (9)$$

By combining equations (5) and (9) and by adopting the boundary conditions at $x = 0$, $c_{H^+}' = c_{H^+}^{\ddagger}$ and $x = x'(t)$, $c_{H^+} = 0$ we obtain the following

$$a_1 = 1$$

$$a_2 = \frac{1}{\text{erf} \sqrt{\frac{\alpha}{D_{H^+}}}}$$

$$x' = \sqrt{4\alpha t} \quad (10)$$

where α = an integration constant. Equation (5) may now be written as

$$c_{H^+} = c_{H_0}^+ - \frac{c_{H_0}^{\ddagger}}{\text{erf} \sqrt{\frac{\alpha}{D_{H^+}}}} \text{erf} \frac{x}{\sqrt{4D_{H^+}t}} \quad (5)$$

The remaining boundary conditions are

at $x = x'(t)$, $c_{B-} = 0$ and

at $x = x'(t)$ the two counteracting diffusion flows are equal, i.e.

$$-D_{H^+} \frac{\partial c_{H^+}}{\partial x} = j_{B-} \quad (11)$$

After differentiation of equation (5) we get the following expression

$$\frac{D_{H^+} c_{H_0}^{\ddagger}}{\sqrt{\pi}} 2 \frac{\exp - \frac{\alpha}{D_{H^+}}}{\text{erf} \sqrt{\frac{\alpha}{D_{H^+}}}} \frac{1}{\sqrt{4D_{H^+}t}} = j_{B-} \quad (12)$$

It is obvious from equation (12) that the integration constant α will depend on the time of electrolysis. In Table II the results of the calculations on the spreading of hydrogen ions are summarised, and in Fig. 1 the curve illustrates its spreading as a function of the time of electrolysis. As a matter of fact, this curve corresponds to the coordinate for pH 3 and does not show the coordinate for the moving boundary itself. However, the absolute difference between these two values is very small as demonstrated by the results in Table II. pH 3 is assumed to be low enough to irreversibly split the haemoglobin molecules.

The amount of hydrogen ions formed during electrolysis is calculated by means of Faraday's law, i.e.

$$n(H^+) = \frac{it\eta}{zF} \quad (13)$$

where $n(H^+)$ = number of hydrogen ions (moles)
 i = anodic current density (2×10^{-2} A/cm²)
 t = time of electrolysis (secs)
 η = current yield (50%)
 $z = 1$
 F = Faraday's constant

These calculations indicate an accumulation of hydrogen ions formed at the anode. One interpretation might have been that the real pH value at the anode surface is still lower than 1. However, a recently finished graduate work at our department gives a more plausible explanation (4). The influence of migration on the spreading of hydrogen ions cannot be neglected and it is clear that in a more accurate analysis of this problem both diffusion and migration must be considered. Thus, the calculated excess of hydrogen ions will in fact be distributed into the tissue by migration due to the electric field. As we have concentration gradients for the ionic species involved one cannot adapt a simple expression to consider the contribution of migration. Instead one should use a set of complete transport equations, which are valid when convection may be neglected (8). As an example, see equation (14).

$$\frac{\partial c_i}{\partial t} = D_i \frac{\partial^2 c_i}{\partial x^2} + \frac{z_i}{|z_i|} u_i \frac{\partial}{\partial x} \left(c_i \frac{\partial \Phi}{\partial x} \right) \quad (14)$$

where u_i = mobility of species i (cm² mole/J sec)
 Φ = electric potential (V)

Table II. Calculated spreading of hydrogen ion in tissue close to a plate anode of platinum after various times of electrolysis and the degree of utilization (α)

t (secs):	10	10 ²	6 × 10 ²	10 ³	2 × 10 ³	5 × 10 ³	8 × 10 ³	10 ⁴
$\alpha \times 10^{-4}$ (cm ² /sec):	3.12	2.00	1.19	1.01	0.72	0.43	0.32	0.27
x' (pH 7) (mm):	1.12	2.83	5.34	6.37	7.58	9.30	10.07	10.41
x (pH 3) (mm):	1.02	2.71	5.22	6.24	7.46	9.17	9.95	10.29
Amount of H ⁺ absorbed × 10 ⁶ (moles):	3.6	11.8	31.5	42	66	123	180	210
Amount of H ⁺ formed × 10 ⁻⁶ (moles):	1.04	10.4	60.4	104	208	520	832	1040
ν (%):	—	—	52	40	32	24	22	20

Another aspect to be considered is the real, total buffer capacity of the tissue. There are slower buffering systems than the hydrogen carbonate system (HCO₃⁻/CO₂), e.g. amino acids fixed to proteins in the tissue. The electrocoagulation of the blood most likely influences the thickness of the reaction zone at the moving boundary, here arbitrarily assumed to be 1 mm. A deeper analysis of the whole problem requires a computerised mathematical model, which is outside the frame of this conference contribution.

CONCLUDING REMARKS

The rate of diffusion of the hydrogen ion seems to be fast enough to ascertain that the acidified zone will reach farther than the chlorinated zone. Various types of tissue have different buffering capacities and the content of covalently bound chlorine may vary depending on the tissue.

It would be desirable to try to determine the extension of the definitely "killed" volume by histological examination of electrochemically treated tissue from animal experiments. Does this borderline coincide with a certain pH level or does the electrochemical treatment exert remaining effects on the tissue beyond the acidified zone? If these so called fields effects are to be evaluated when considering the total, long-term effects of electrochemical treatment, a higher degree of resolution must be adopted to describe the tissue as an electrolyte.

It may be necessary to deal with this problem in relation to the size of living cells and then define the pathways of the current as thin tracks of interstitial fluid between the cells constituting the tissue.

The toxic properties of the chlorine close to the anode and of the hydrogen chloride within a broader zone may be enough to explain the clinical effects of this electrochemical method for treatment of tumours. The formation of radicals or other inter-

mediates in the anodic reactions does not seem to account satisfactorily for these beneficial, local effects.

SUMMARY

In the electrochemical treatment of tissue with direct current the main reactions at the anode are the formation of oxygen in addition to acidification due to liberated hydrogen ions, and formation of chloride, if platinum is used as anode material. At the cathode hydrogen is formed and hydroxide ions are liberated. Calculations have been made for the two major anodic reactions. As a first approximation just one-dimensional diffusion is considered corresponding to the use of plate electrodes. It appears from these calculations that the liberated hydrogen ions determine the extension of the locally destroyed zone around the anode. The destructive effect of chlorine probably occurs in an inner zone close to the anode.

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