ESTIMATION OF THE FILTRATION CONSTANT OF DOG SUBMAXILLARY GLAND EPITHELIA

—AN APPROXIMATE VALUE OF HYDRAULIC CONDUCTIVITY—

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Summary To estimate the hydraulic conductivity of dog submaxillary gland, an attempt was made to determine filtration constants of the glandular epithelium by analyzing the decay curve of the stop-flow intraluminal pressure.

The time course of the decay of intraluminal pressure after cessation of the secretory stimulation was found to be expressed as an algebraic sum of two exponential functions of time, one having the rapid component and the other having the slow component:

$$P = A e^{-\lambda_1 t} + Be^{-\lambda_2 t}$$

The rapid component is attributable to the relaxation of the myoepithelium because the rate constant of the rapid component ($\lambda_2$) is in good accordance with the rate constant of the relaxation of the myoepithelium. The rate constant of the slow component ($\lambda_1$) is deduced theoretically to be a product of the filtration constant and a coefficient of volume elasticity of the gland. The value of $\lambda_1$ was found experimentally to be 0.00512 sec$^{-1}$, and the coefficient of volume elasticity obtained by measuring the intraluminal pressure elevated by retrograde injections of fluid was 1.52 mmHg·g-gland·µl$^{-1}$. From these results, the filtration constant of dog submaxillary gland was estimated to be 0.0033 µl·sec$^{-1}$·mmHg$^{-1}$·g-gland$^{-1}$ on the average. Recalculating the value on the basis of the surface area of the acinus per unit gland weight, a value of the filtration constant or an approximate value of the hydraulic conductivity of the acinal surface was calculated to be $6 \times 10^{-11}$ cm$^3$·sec$^{-1}$·dyne$^{-1}$. The numerical values of the parameters described above may be applicable under similar experimental conditions to those used in the present study.

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In a previous study (IMAI et al., 1973) of our group, it was found that in dog's submaxillary glands the osmotic concentration of the secretion under the influence of a high hydrostatic pressure was hypertonic, and that the glandular epithelium had a semipermeable property. As osmotic flow is a basic process in exocrine gland secretion, hydraulic conductivity of the glandular epithelium is considered to be one of the important factors for a quantitative analysis of the secretory mechanism for water (KEDEM and KATCHALSKY, 1958).

In this study, it was attempted to estimate the filtration constant of the glandular epithelium in order to know the approximate value of the hydraulic conductivity of the tissue. For this purpose, an analysis of the decay curve of the stop-flow intraluminal pressure was made in dog submaxillary gland. The reason for the use of such a technique is that the gland is so complicated that the deduction of the filtration constant from a simple relation between pressures and flow rates is very difficult (LUBARSKY and NICOLL, 1968; LANGLEY and BRAWN, 1961). The luminal pressure is maintained by both the elastic recoil of the entire glandular tissue after an expansion by a volume change in the lumen and the active tension of the myoepithelium surrounding the acinus (EMMELIN et al., 1969). Therefore the decay of luminal pressure in the closed system elevated by the secretory stimulation is mainly due to both the relaxation of tension resulting from the back filtration of the fluid through the glandular tissue and the relaxation of the myoepithelium. The filtration constant was obtained from the former factor.

METHODS

Dogs were anesthetized by intravenous injections sodium thiopental (30–40 mg/kg body weight). The submaxillary gland was dissected and the excretory duct was connected through a three-way stopcock to a pressure transducer (Kyo- wa Dengyo, MP-28; volume displacement: 4.45×10⁻³ mm³/360 mmHg). The connection was carefully made to prevent any leakage of fluid from the trans-
ducer and the stopcock system. The tetanic stimulation of the chorda tympani
(20 Hz, 3 volts, and pulse duration 5 msec) was used as the secretory stimulation
for a few minutes, and the secretory pressure in the closed system, which con-
sisted of the glandular lumen and the pressure transducer, was recorded during
and after stimulation. The pressure was also measured 10 sec after retrograde
injections of various amounts of mineral oil to obtain the coefficient of volume
elasticity of the glandular tissue. The experimental setup is shown diagramati-
cally in Fig. 1.

RESULTS

When the luminal pressure in the closed system, which consisted of the
glandular lumen and a pressure transducer, was raised by a stimulation of the
chorda tympani, the secretory pressure reached at a steady and maximum value
within a minute, the value ranging from 200 to 300 mmHg. The recording of
the secretory pressure was continued for a sufficiently long period of time after
the cessation of the stimulation, and one of the typical records is shown in Fig. 2.
When the decay of the luminal pressure was plotted on a semilogarithmic chart,
the curve could be fitted with a double exponential line, namely, the decay curve
could be expressed as an algebraic sum of two exponential terms:

\[ P = Ae^{-\lambda_1 t} + Be^{-\lambda_2 t}. \]  

An example of such analysis is shown in Fig. 3, in which the decay curve is ex-
pressed as \( P = 129e^{-0.00066t} + 130e^{-0.136t} \). For ten observations, the range of
\( \lambda_1 \) was 0.0016–0.0083 sec\(^{-1}\) and that of \( \lambda_2 \) was 0.05–0.15 sec\(^{-1}\), and \( A \) and \( B \) values
were both in the range of 80–150 mmHg.

The coefficient of volume elasticity of the gland was obtained from the
intraluminal pressure measured at 10 sec after the retrograde injection of a known

![Fig. 2. Time course of the secretory pressure during the chorda stimulation (26 sec) and
the decay process of the pressure after cessation of the stimulation.](image)
Fig. 3. A semilogarithmic plot of the time course of the decay of the luminal pressure. The curve can be expressed as an algebraic sum of two exponential terms.

$$P = 130e^{-0.036t} + 129e^{-0.0066t}$$

Fig. 4. The relationships between the luminal pressure and the fluid volume injected retrogradely in three typical cases. The coefficient of volume elasticity was estimated from the slope of the curves.

V: volume of mineral oil injected retrogradely

P: duct pressure of gland
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volume of mineral oil from the duct using the following equation:

\[ dP_1 = kdV, \]

where \( dP_1 \) is the change in pressure (in mmHg), \( dV \) the volume change in the glandular lumen (in \( \mu l \cdot g\)-gland\(^{-1} \)) and \( k \) the coefficient of volume elasticity (in mmHg \cdot g\)-gland \cdot \( \mu l \)^{-1}). Figure 4 shows the relationship between the intraluminal pressure and the volume of mineral oil injected retrogradely, and based on the result, the coefficient of volume elasticity \( (k) \) of the gland was calculated. The filtration constant of the glandular tissue \( (K_f) \) was obtained by dividing the rate constant of the slow component of the decay curve \( (\lambda_1) \) by the coefficient of volume elasticity \( (k) \). The values of \( \lambda_1 \) and \( k \) and also calculated values of \( K_f \) for ten measurements are summarized in Table 1 together with means and standard deviations.

Table 1. The values for the rate constant of the slow component of the decay curve \( (\lambda_1) \), the coefficient of volume elasticity of the gland \( (k) \) and calculated filtration constant of the glandular tissue \( (K_f) \).

<table>
<thead>
<tr>
<th>No.</th>
<th>( \lambda_1 ) sec(^{-1} )</th>
<th>( k ) mmHg \cdot g)^{-1} \cdot ( \mu l )(^{-1} )</th>
<th>( K_f ) \mu l(^{-1} \cdot \text{mmHg}^{-1} \cdot g^{-1} )</th>
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<td>0.0016</td>
<td>0.80</td>
<td>0.0020</td>
</tr>
<tr>
<td>2</td>
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<td>0.0027</td>
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<td>0.0031</td>
<td>1.20</td>
<td>0.0026</td>
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<td>1.70</td>
<td>0.0034</td>
</tr>
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<td>7</td>
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<td>0.0040</td>
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<tr>
<td>10</td>
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<td>0.0052</td>
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<tr>
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<td>1.52</td>
<td>0.0033</td>
</tr>
<tr>
<td>S. D.</td>
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<td>0.459</td>
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DISCUSSION

The pressure in the glandular lumen is considered to be proportional to the tension of the glandular wall so long as the pressure is not too high. Within the physiological limit, the increased tension of the glandular wall due to volume changes in the lumen may be expressed by the following two additive factors: one is the passive tension balanced with the elastic recoil of the elastic tissue and the other the active tension of the myoepithelium surrounding the acinus. Hence, the luminal pressure can be expressed by:

\[ P = P_1 + P_2, \]

where \( P \) is the intraluminal pressure, \( P_1 \) the passive pressure originated by the passive tension which correspond to \( dP_1 \) in Eq (2) and \( P_2 \) the active pressure
exerted by the active tension of myoepithelial contraction. When the gland is stimulated, passive tension may be elevated by secretion of primary saliva into the lumen, and the active tension may also be elevated by contraction of the myoepithelium. However, in a later phase of pressure decay after the cessation of stimulation, it may be assumed that the secretion of saliva ceases and the active tension of the myoepithelium become also negligible because the decay originated by the relaxation of the myoepithelium is so rapid (EMMELIN et al., 1969). Under such conditions, the decrease of the intraluminal pressure should be mainly due to loss of saliva through the acinar and the intercalated duct wall. Therefore, it may be assumed that the rate of fluid loss is due to back filtration caused by the intraluminal pressure, and one can write

\[ -\frac{dV}{dt} = K_f \cdot P, \]

where \(-dV/dt\) is the rate of volume loss, \(P\) is the intraluminal pressure and \(K_f\) is the filtration constant per unit gland weight. Using Eq. (2), the above equation can be transformed to

\[ \frac{dP}{P} = - k \cdot K_f \cdot dt. \]

The later part of the decay of the luminal pressure was actually exponential and the rate constant obtained \((\dot{\lambda}_1)\) should correspond to \(k \cdot K_f\). Since the coefficient of volume elasticity \((k)\) of the gland was determined experimentally, \(K_f\) can be calculated using the mean value of \(\dot{\lambda}_1\) and \(k\). It was calculated to be \(0.0033 \pm 0.00094 \mu l \cdot \text{sec}^{-1} \cdot \text{mmHg}^{-1} \cdot \text{g-gland}^{-1}\) (Table 1).

Further discussion should be made on the reason by which the decay curve can be expressed by an algebraic sum of two exponential terms. The relaxation of the active tension exerted by the myoepithelium is inferred to fall exponentially, like the fall in tension of the skeletal muscle during the isometric relaxation (JEwELL and WILKIE, 1960). Therefore the active pressure \(P_2\) in Eq. (3) during relaxation process may be assumed by the following equation:

\[ P_2 = P_2(0)e^{-\dot{\lambda}_2 t}. \]

Here \(P_2(0)\) is \(P_2\) at \(t=0\), \(\dot{\lambda}_2\) is the rate constant. The values of \(\dot{\lambda}_2\) obtained on the basis of our data are in good accordance with the rate constant (about 0.06–0.1 sec\(^{-1}\)) of the relaxation of the myoepithelium which can be deduced from the data of EMMELIN et al. (1969). Therefore the decay process of the luminal pressure can be expressed by the next Eq. using Eqs. (2), (3), and (6):

\[ P = kV + P_2(0)e^{-\dot{\lambda}_2 t}. \]

Substituting (7) into (4), one can obtain

\[ -\frac{dV}{dt} = K_f(kV + P_2(0)e^{-\dot{\lambda}_2 t}). \]
Eq. (8) can be transformed as follows:

\[ kK_f V + \frac{dV}{dt} = -K_f P_{2(0)} e^{-\lambda_2 t}, \]

then

\[ \frac{d}{dt} (V e^{kK_f t}) = -K_f P_{2(0)} e^{(kK_f - \lambda_2) t}. \]  \hspace{1cm} (9)

Eq. (9) can be integrated as follows:

\[ V e^{kK_f t} = -\frac{K_f P_{2(0)}}{kK_f - \lambda_2} e^{(kK_f - \lambda_2) t} + \text{const.} \]  \hspace{1cm} (10)

At \( t=0 \),

\[ V_0 = -\frac{K_f P_{2(0)}}{kK_f - \lambda_2} + \text{const.} \]

Therefore Eq. (10) becomes

\[ V = -\frac{K_f P_{2(0)}}{kK_f - \lambda_2} e^{-\lambda_2 t} + \frac{K_f P_{2(0)}}{kK_f - \lambda_2} e^{-kK_f t} + V_0 e^{-kK_f t}. \]  \hspace{1cm} (11)

Substituting (11) into (7), one obtains

\[ P = \left( \frac{K_f P_{2(0)}}{kK_f - \lambda_2} + kV_0 \right) e^{-kK_f t} + \frac{\lambda_2 P_{2(0)}}{\lambda_2 - kK_f} e^{-\lambda_2 t}. \]  \hspace{1cm} (12)

Using the relation \( P_{1(0)} = kV_0 \), which is derived from Eq. (2) one can write

\[ P = \left( P_{1(0)} - \frac{kK_f P_{2(0)}}{\lambda_2 - kK_f} \right) e^{-kK_f t} + \frac{\lambda_2 P_{2(0)}}{\lambda_2 - kK_f} e^{-\lambda_2 t}, \]  \hspace{1cm} (13)

and if \( \lambda_2 \gg kK_f \), Eq. (13) becomes

\[ P = P_{1(0)} e^{-kK_f t} + P_{2(0)} e^{-\lambda_2 t}. \]  \hspace{1cm} (14)

Then the algebraic sum of two different exponential terms in our experimental results as seen in Eq. (1) indeed corresponds to Eq. (14). So it is shown that the rate constant in the slow phase of decay curve, \( \lambda_1 \), is \( kK_f \) as already shown in Eq. (5) and the rate constant in the rapid phase, \( \lambda_2 \), is the rate constant attributable to the activity of the myoepithelium.

The hydraulic conductivity is defined as the conductivity of a tissue or membrane to water which is driven by both hydrostatic and osmotic pressure (KeDEM and KATCHALSKY, 1958). On the other hand, the filtration constant used in this study was measured by the water flow driven by hydrostatic pressure only. However, if the hydraulic conductivity at the striated part and the main duct system can be assumed to be negligible and if the gradient of osmotic concentration across the epithelium of the acinus and the intercalated duct can be assumed to be negligible, the filtration constant obtained \( (K_f) \) will become the hydraulic con-
ductivity of the epithelium of the acinus and the intercalated duct. The first assumption that the duct system should have a low hydraulic conductivity may probably be reasonable, because the ratio of osmotic concentration of saliva to that of plasma was less than 0.5 in the present experiment, and thus the water permeability in the duct system as discussed in the previous report was relatively small (Imai et al., 1972). On the other hand, the latter assumption of negligible concentration gradients across the acinar part under a high hydrostatic pressure of lumen may apparently contradict with our previous report (Imai et al., 1973). However, it may be possible to use the filtration constant as obtained in this study as an approximate value for the hydraulic conductivity of the acinar part, although some amendment should be done in future. When one assumed that water pass through the outer surface of the acinus and the surface area was calculated to be about 600 cm²/g gland on an assumption that the salivary gland is packed with acini with 50 µ of diameter, an approximate value for the hydraulic conductivity of the surface barrier was found to be about $0.6 \times 10^{-11}$ cm³ sec⁻¹ dyne⁻¹. This value is in good agreement with hydraulic conductivities of various biological cell membrane reported by various investigators: $0.92 \times 10^{-11}$ for human red cells (Sidell and Solomon, 1957), $2.5 \times 10^{-11}$ for blood capillary wall (Pappenheimer, 1953), $0.5 \times 10^{-11}$ for the gall bladder of the rabbit (Diamond, 1962), 0.67 and $1.55 \times 10^{-11}$ for rabbit corneal epithelium and endothelium (Mishima and Hedbys 1967), and 15.0 and $1.6 \times 10^{-11}$ cm³ sec⁻¹ dyne⁻¹ for rat proximal and distal tubules (Persson and Ulfendahl, 1970; Persson, 1970). It seems that this agreement may be due to a common property of biological cell membranes against water permeation.

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REFERENCES


