CONCERNING THE RELATIONSHIP BETWEEN THE STRENGTH OF ACIDS AND THEIR CAPACITY TO PRESERVE NEUTRALITY.

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In the light of relationships already discussed concerning the mechanism for the preservation of neutrality in the animal organism, it is interesting to consider what the principles underlying the regulation of the reaction of a simple solution may be, for in this way it may be possible to discover how closely the physiological mechanism approaches to ideal conditions.

According to the mass law, in the pure solution of a weak acid, $\text{IIA}$, the relationship holds, $k \cdot (\text{HA}) = (\hat{H}) \cdot (\bar{A})$, where $k$ is the ionization constant of the acid and the enclosed quantities represent the concentrations of the respective substances. This equation may be more conveniently written

$$ (\hat{H}) = k \cdot \frac{(\text{HA})}{(\bar{A})}. $$

If now the sodium salt, or other salt with a strong base, of the acid be introduced into such a solution as is above considered, it is evident that we shall have the following condition. The concentration of unionized molecules of acid will be almost precisely equal to the total amount of acid present, while the concentration of the ions $(\bar{A})$, much increased because of the presence of the salt, will be equal to the concentration of the salt multiplied by its degree of dissociation. This latter factor, varying with the strength of the acid and the concentration of the salt, will usually not be less than 0.6.

We may therefore write the equation, $-$

1 See Henderson and Black: This journal, 1907, xviii, pp. 250-255.
where $K$ is the ionization constant of the acid divided by the degree of ionization of the salt, and $HA$ and $MA$ represent the amounts of acid and salt present in the solution.

From an inspection of the above equation it is easy to see that if $K$ is equal to the hydrogen ionization at neutrality, approximately $1 \times 10^{-7}$, the conditions will be exceedingly favorable for the maintenance of neutrality. For at neutrality the ratio between acid and salt must then be equal to 1, and accordingly the addition of acid or alkali will here influence but slightly the magnitude of the ratio, at least at first, thereby influencing but slightly the hydrogen ionization.²

It may readily be shown that in general the preservation of neutrality within any range of acidity and alkalinity is most efficient when $K$ is equal to the square root of the water constant.

Let

$$K = k \cdot \sqrt{C_{H_{2}O}}, \text{ when } C_{H_{2}O} \text{ is the water constant.}$$

Then

$$(H) = \frac{HA}{MA} \cdot k \cdot \sqrt{C_{H_{2}O}},$$

but

$$\langle H \rangle \equiv \frac{C_{H_{2}O}}{\langle OH \rangle};$$

hence

$$\langle OH \rangle = \frac{MA}{HA} \cdot \frac{1}{k} \cdot \sqrt{C_{H_{2}O}}.$$  

Let

$$\frac{HA}{MA} = R \text{ (the ratio between acid and salt).}$$

Then

(I) \hspace{1cm} \langle H \rangle = R \cdot k \cdot \sqrt{C_{H_{2}O}}.$$ 

(II) \hspace{1cm} \langle OH \rangle = \frac{1}{R} \cdot \frac{1}{k} \cdot \sqrt{C_{H_{2}O}}.$$

The rate of change in hydrogen ionization as $R$ changes may be found by differentiating equation (I) with respect to $R$, and

² This conclusion, developed in wholly different connections, was presented at a meeting of the Physico-Chemical Club of Boston and Cambridge simultaneously by E. W. Washburn and myself; see E. W. Washburn, Journal of the American Chemical Society, 1908, xxx, p. 31.
similarly the rate of change in hydroxyl ionization as \( \frac{1}{R} \) changes by differentiating equation (II) with respect to \( \frac{1}{R} \). Thus we obtain the equations,

\[
\frac{d\left(\frac{1}{R}\right)}{dR} = k \cdot \sqrt{C_{Hx_0}},
\]

(III) \[
\frac{d\left(\frac{1}{R}\right)}{d\frac{1}{R}} = \frac{1}{k} \cdot \sqrt{C_{Hx_0}}.
\]

(IV)

Clearly, for the most efficient preservation of neutrality, the sum of these two rates of change must be as small as possible. Representing the sum of the rates of change by \( S \), we may write the equation,

\[
S = k \cdot \sqrt{C_{Hx_0}} + \frac{1}{k} \cdot \sqrt{C_{Hx_0}}.
\]

(V)

The condition that \( S \) may be as small as possible may be found by differentiating with respect to \( K \) and putting the derivative equal to 0; that is to say,

\[
\left(1 - \frac{1}{k^2}\right) \cdot \sqrt{C_{Hx_0}} = 0,
\]

whence

\[
(VI) \quad k = 1.
\]

\[
(VII) \quad \begin{cases} K = \sqrt{C_{Hx_0}} \\ K_{a0} = 1 \times 10^{-7} \end{cases}
\]

This theoretical conclusion may be readily verified with a moderate but sufficient degree of accuracy by simple titration experiments with properly chosen indicators, in accordance with the recent studies of Salm.\(^3\) Thus, using solutions of the acids mono-sodium phosphate, carbonic acid, acetic acid, hydrogen sulphide, picolinic acid, boric acid, and phenol, I have found that to pass from one standard coloration with rosolic acid to another standard coloration, it is necessary to use the greatest amount of alkali for hydrogen sulphide; mono-sodium phosphate and carbonic acid follow closely, and the other substances at a greater distance.

The experiments were carried out by simple titration, using solutions that varied between 0.04 N and 0.12 N\(^4\) in individual cases.

\(^3\) E. SALM: Zeitschrift für physikalische Chemie, 1906, lvii, p. 471.

\(^4\) The acid substances are all regarded as mono-basic.
The colors were always compared with standard colors given by mixtures of mono- and di-sodium phosphate, and at least three determinations were made in every case. No difficulty was experienced save in the case of hydrogen sulphide, where it was finally found better to titrate from the color with neutral red given by a solution of mono- and di-sodium phosphates in the ratio 1:1 to the color given by a similar solution in the ratio 1:6.7 with rosolic acid. The data of these determinations are presented as an example of the perfectly simple procedure:

\[
\begin{align*}
\text{NaOH} & \quad 0.102 \text{ N.} \\
\text{NaH}_2\text{PO}_4 & \quad 0.082 \text{ N.} \\
\text{H}_2\text{S} & \quad 0.045 \text{ N.}
\end{align*}
\]

<table>
<thead>
<tr>
<th>First color.</th>
<th>Second color.</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 c.c. NaH(_2)PO(_4)</td>
<td>4.00 c.c. NaOH</td>
</tr>
<tr>
<td>10 c.c. H(_2)S</td>
<td>1.55 c.c. NaOH</td>
</tr>
<tr>
<td>10 c.c. H(_2)S</td>
<td>1.15 c.c. NaOH</td>
</tr>
<tr>
<td>10 c.c. H(_2)S</td>
<td>1.15 c.c. NaOH</td>
</tr>
<tr>
<td>10 c.c. H(_2)S</td>
<td>1.35 c.c. NaOH</td>
</tr>
</tbody>
</table>

On the average, as appears from the above table, the first color was given by a solution containing hydrogen sulphide and its acid sodium salt in the ratio 1:0.42, and the second color by a similar mixture in the ratio 1:2.5.

In the following table are presented the results of these titrations, expressed in the form of the relative amounts of alkali required for equivalent solutions of the different acids to pass from the one standard coloration to the other, the amount of alkali required for mono-sodium phosphate being used as the basis for comparison.

<table>
<thead>
<tr>
<th>Acid.</th>
<th>(A' \times 10^7)</th>
<th>Alkali required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenol</td>
<td>0.0013</td>
<td>0.01</td>
</tr>
<tr>
<td>Boric acid</td>
<td>0.017</td>
<td>0.08</td>
</tr>
<tr>
<td>Hydrogen sulphide</td>
<td>0.57</td>
<td>1.10</td>
</tr>
<tr>
<td>Mono-sodium phosphate</td>
<td>2.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Carbonic acid</td>
<td>3.0</td>
<td>0.72</td>
</tr>
<tr>
<td>Picolinic acid</td>
<td>18.0</td>
<td>0.30</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>180.0</td>
<td>0.03</td>
</tr>
</tbody>
</table>

These relationships may readily be compared with the theory presented above by a slightly different analysis of the relationships.
Strength of Acids and Neutrality.

\[
\dot{H} = \frac{HA}{MA} \cdot k \cdot \sqrt{C_{H_2O}}
\]

may conveniently be written

\[
\dot{H} = \frac{HA}{MA} \cdot k \cdot 10^{-7}.
\]

Let

\[
HA + MA = 1
\]

\[
\dot{H} = \frac{1 - MA}{HA} \cdot k \cdot 10^{-7}.
\]

Let it be required to find the amount of alkali, \(X\), required to convert a mixture of acid and salt of hydrogen ionization \(2 \times 10^{-7}\) into a mixture of hydrogen ionization \(0.5 \times 10^{-7}\).

\[
\frac{1 - (MA)_1}{(MA)_1} \cdot k \cdot 10^{-7} = 2 \cdot 10^{-7}.
\]

\[
\frac{1 - (MA)_2}{(MA)_2} \cdot k \cdot 10^{-7} = \frac{1}{2} \cdot 10^{-7}.
\]

\[
2 (MA)_1 + k(MA)_1 = k.
\]

\[
\frac{1}{2} (MA)_2 + k(MA)_2 = k.
\]

\[
(MA)_1 = \frac{k}{k + 2}.
\]

\[
(MA)_2 = \frac{k}{k + \frac{1}{2}}.
\]

\[
x = (MA)_2 - (MA)_1 = \frac{k}{k + 2} - \frac{k}{k + \frac{1}{2}}.
\]

\[
x = \frac{3}{5 + 2 \left( \frac{k + \frac{1}{2}}{k} \right)}.
\]

With the aid of this equation the following table is constructed:

<table>
<thead>
<tr>
<th>(k)</th>
<th>(x)</th>
<th>(k)</th>
<th>(x)</th>
<th>(k)</th>
<th>(x)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1 \times 10^{-8})</td>
<td>0.0002</td>
<td>(4 \times 10^{-7})</td>
<td>0.179</td>
<td>(5 \times 10^{-8})</td>
<td>0.325</td>
</tr>
<tr>
<td>(1 \times 10^{-4})</td>
<td>0.002</td>
<td>(3 \times 10^{-7})</td>
<td>0.214</td>
<td>(4 \times 10^{-8})</td>
<td>0.312</td>
</tr>
<tr>
<td>(1 \times 10^{-9})</td>
<td>0.021</td>
<td>(2 \times 10^{-7})</td>
<td>0.263</td>
<td>(3 \times 10^{-8})</td>
<td>0.285</td>
</tr>
<tr>
<td>(1 \times 10^{-10})</td>
<td>0.089</td>
<td>(1 \times 10^{-7})</td>
<td>0.324</td>
<td>(2 \times 10^{-8})</td>
<td>0.239</td>
</tr>
<tr>
<td>(9 \times 10^{-11})</td>
<td>0.97</td>
<td>(9 \times 10^{-8})</td>
<td>0.329</td>
<td>(1 \times 10^{-9})</td>
<td>0.156</td>
</tr>
<tr>
<td>(8 \times 10^{-7})</td>
<td>0.107</td>
<td>(8 \times 10^{-8})</td>
<td>0.332</td>
<td>(1 \times 10^{-9})</td>
<td>0.025</td>
</tr>
<tr>
<td>(7 \times 10^{-7})</td>
<td>0.119</td>
<td>(7 \times 10^{-8})</td>
<td>0.333</td>
<td>(1 \times 10^{-10})</td>
<td>0.003</td>
</tr>
<tr>
<td>(6 \times 10^{-7})</td>
<td>0.134</td>
<td>(6 \times 10^{-8})</td>
<td>0.332</td>
<td>(1 \times 10^{-11})</td>
<td>0.0003</td>
</tr>
<tr>
<td>(5 \times 10^{-7})</td>
<td>0.153</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(k\) = ionization constant of acid.

\(x\) = neutralizing power.
This table may be graphically presented. In the accompanying diagram the continuous line represents the calculated relationships of the table, and the dotted line the experimentally determined relationships. The values of \( x \) in the table are plotted as ordinates, and values of \( k \) are plotted logarithmically as abscissas. It is evident that the accord between theory and observation is very good.

This quantitative analysis, theoretical and experimental, of the efficiency of neutrality preservation amply justifies the belief that in the organism carbonic acid and phosphoric acid can serve very efficiently to preserve neutrality, and it shows that they possess high qualifications for the carrying out of this function. Needless to say, the conditions within the organism are more complicated than those in simple solution, but such simple solutions as these which we are here considering furnish evidence which is directly applicable to the true solutions of the organism. The complications involved in these equilibria by the complexity of the organization of the animal body do indeed serve to modify conditions, in part by furnishing reservoirs of supply and vehicles of escape for the components of the simple systems. But, as I hope later to show, in great part these modifications of the conditions of equilibrium in the body serve greatly to increase the efficiency of carbonates and phosphates in preserving neutrality.

**Summary.**

It appears that acids whose ionization constant is nearly equal to the hydrogen ionization at neutrality possess, with the help of their salts, a great capacity for preserving neutrality in simple solution, while other acids are in like concentration of relatively very little

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\( ^6 \) For purposes of comparison these are brought to the scale of the calculated relationships by assuming for mono-sodium phosphate the correct value. This assumption is amply justified by experiments now being carried on in this laboratory. This paper is, however, concerned only with relative magnitudes.
effect in this matter. Other things being equal, the greatest possible efficiency in preserving neutrality, on both sides of the neutral point, is possessed by that acid whose ionization constant is precisely equal to the hydrogen ionization of water divided by the degree of ionization of the salt. Clearly, then, the ionization constant of carbonic acid, $3 \times 10^{-7}$, and of the ion $H_2PO_4$, $2 \times 10^{-7}$, gives them nearly the greatest possible efficiency for preserving neutrality in simple solution.