INTRODUCTION

In the first presentation in this series, three common topics in hemodialysis were discussed. In this presentation, the topic is buffers and how they work. An understanding of buffers requires two mathematical tools: the equilibrium constant ($K_{eq}$ and $pK$), and the pH. A working knowledge of logarithms is necessary in order to use these tools.

For a logarithm refresher, refer to a college algebra text. For a general chemistry reference, we recommend White, Erickson and Stevens.

$pK$

Some chemical reactions under normal conditions go nearly to completion. An example is the ionization of sodium chloride ($NaCl \rightarrow Na^+ + Cl^-$), which has been previously discussed with regard to its electrolyte properties.

Many other reactions, however, reach an equilibrium consisting of finite amounts of both reactants and products. Equation (1) described the relationship between four species at equilibrium:

$$A + B \rightleftharpoons C + D$$

The arrows in both directions indicate that the reaction is reversible, at least to some degree.

If $A$ and $B$ are initially reacted together, the rate of the reaction is proportional to the concentrations of both $A$ and $B$. This relationship is shown by equation (2):

$$r_f = k_f[A][B]$$

The notation $r_f$ is the rate of the forward reaction, $k_f$ is a constant, and the brackets denote concentrations in moles per liter ($M/L$). Since the relationship is reversible, a similar equation describes the backward reaction:

$$r_b = k_b[C][D]$$

The notation $r_b$ is the rate of the backward reaction and $k_b$ is a different constant. Equations (2) and (3) show that the rates of the forward and backward reactions are proportional to the concentrations of the reacting species.

At equilibrium, the concentrations of $A$, $B$, $C$, and $D$ are constant. Therefore, the forward and backward reaction rates must be equal. Equations (2) and (3) can be set equal to each other and rearranged to place all of the concentrations on one side of the equation:

$$k_f[A][B] = k_b[C][D]$$

At equilibrium, equation (4) is true, regardless of the amount of $A$ and $B$ that were initially reacted together. This special relationship is called $K$, the *equilibrium constant*. It is defined in equation (5):

$$K = \frac{[C][D]}{[A][B]}$$
The subscript denotes that the reactants of this reaction are A and B.

If an equilibrium mixture exists as nearly all product, the $K$ value will be very large; if the mixture exists as nearly all reactant, the $K$ value will be very small. To facilitate the calculation of these very large and small numbers, a logarithmic shorthand, the $pK$ is used:

$$\text{(6)} \quad pK = -\log_{10} K$$

This shorthand is very useful. If a reaction equilibrium mixture exists as reactant, such that the $K = 1.0 \times 10^{-5}$, the $pK$ of this reaction is 5. This notation eliminates the use of both very small numbers and negative exponents. Few reactions with large $K$ values are usually measured since the amount of reactant present is very small. These reactions, however, have large $K$ values, and negative $pK$ values.

The ionization of acetic acid (symbol $\text{HAc}$) into hydrogen ion $^+$ and acetate (symbol $\text{Ac}^-$) illustrates the use of $K$ and $pK$.

$$\text{(7)} \quad \text{HAc} \rightleftharpoons H^+ + \text{Ac}^-$$

At equilibrium, the equilibrium constant $K_{\text{HAc}}$ has been measured.

$$\text{(8)} \quad K_{\text{HAc}} = \frac{[H^+][\text{Ac}^-]}{[\text{HAc}]} = 1.74 \times 10^{-5}$$

Equation (6) can be used to calculate the $pK$:

$$pK_{\text{HAc}} = -\log_{10}(1.74 \times 10^{-5})$$

$$pK_{\text{HAc}} = -[\log_{10}(1.74) + \log_{10}(10^{-5})]$$

$$pK_{\text{HAc}} = -[0.24 - 5.00]$$

$$\text{(9)} \quad pK_{\text{HAc}} = 4.76$$

Since the $K$ value was very small ($10^{-5}$), the equilibrium mixture was mostly reactant. The $pK$ value is large and positive. The $pK$ notation has eliminated the use of small $K$ values and negative exponents. A use of the $pK$ will be shown in the section on buffers.

**pH**

Pure water can normally be considered to be free of ions. However, close inspection reveals that water does ionize to a slight degree.

$$\text{(10)} \quad \text{H}_2\text{O} \rightleftharpoons H^+ + \text{OH}^-$$

$$\text{(11)} \quad K_w = [H^+][\text{OH}^-] = 10^{-14} \text{ at } 25°C$$

$$\text{(12)} \quad pK_w = -\log_{10}K_w = -\log_{10}(10^{-14})$$

$$\text{(13)} \quad pK_w = 14$$

The very small degree to which water ionizes is reflected by the large $pK$ value of 14. In pure water, there is no other source of acid or base, so $[H^+] = [\text{OH}^-] = 10^{-7}$. Since these numbers are so small, a shorthand notation is also used for the $H^+$ and $\text{OH}^-$ concentrations. These notations, the $pH$ and $pOH$, are defined in equations (14) and (15).

$$\text{(14)} \quad pH = -\log_{10}[H^+]$$

$$\text{(15)} \quad pOH = -\log_{10}[\text{OH}^-]$$

For pure water, therefore, $pH = 7.0$. Acidic solutions contain more than $10^{-7}$ M/L of $H^+$; the $pH$ of acidic solutions is less than 7.0. Basic, or alkaline, solutions contain less than $10^{-7}$ M/L of $H^+$; the $pH$ is greater than 7.0.

Since equation (11) is true for all solutions at 25°C, the $[H^+]$ can be calculated if the $[\text{OH}^-]$ is known. This is the case in strong solutions of some hydroxides. A simpler way of making this comparison uses the $pH$ and $pOH$. It is found by taking the negative logarithm of both sides of equation (11), thus:

$$\text{(16)} \quad -\log_{10} K_w = -\log_{10}[H^+] -\log_{10}[\text{OH}^-]$$
The left hand side of equation (16) is the $pK_w$ and the right hand side is the pH and pOH.

\[ pK_w = pH + pOH \]  

This restates the dissociation of water in terms of the pH and pOH. It is used to calculate the pH of hydroxide solutions. For example, in a 0.001 M/L solution of NaOH, the pOH is 3.0 (equation 15). Since $pK_w = 14$, these values can be substituted into equation (17) to find that the pH of this solution is 11.0.

It is important to note that a change of one pH unit represents a 10-fold change in $[H^+]$.

BUFFERS

Buffers are solutions that resist a pH change when $H^+$ is added or removed. The acetic acid-acetate buffer system is commonly used in dialysis bath solutions. This system is described in equation (18):

\[ HAc \rightarrow H^+ + Ac^- \]

If $H^+$ is added to this equilibrium mixture, the reaction goes to the left. Acetate and $H^+$ are consumed; undissociated acetic acid is produced. This shift consumes some of the added $H^+$ and minimizes the pH change that occurs.

Similarly, if $H^+$ is removed from the solution, the reaction goes to the right: acetate and $H^+$ are released. The added $H^+$ partially compensates for the $H^+$ that was removed. The pH effect is minimized.

If a buffer solution is needed to provide for both conditions of added or removed acid, then the buffer must be present in both its acid and base forms. There would then be a source of which ever species is needed in the equilibrium shift.

Buffers have a pH value at which they are most powerful and most useful. The following steps illustrate the determination of the optimum pH:

\[ K_{HAc} = \frac{[H^+][Ac^-]}{[HAc]} \]

Equation (19) can be rearranged so the $H^+$ term is on the left hand side of the equation.

\[ [H^+] = K_{HAc} \frac{[HAc]}{[Ac^-]} \]

By taking the negative logarithm of both sides of equation (20), the following relationship is found:

\[ -\log_{10}[H^+] = -\log_{10} K_{HAc} -\log_{10} \frac{[HAc]}{[Ac^-]} \]

The term on the left hand side of the equation is the pH. The first term on the right hand side is the $pK$. By making these substitutions, the relationship becomes:

\[ pH = pK -\log_{10} \frac{[HAc]}{[Ac^-]} \]

If the concentrations of the acid form and the base form are equal, the logarithmic term in equation (22) is zero. The pH of this solution is equal to the $pK$.

The acetic acid-acetate buffer system is most useful where the pH of the solution is near its $pK$. When this is true, the buffer can accommodate either added or removed acid. The $pK$, however, is 4.76, indicating that the optimum pH for this buffer is between pH values of 4 and 5.

Since the physiological pH is 7.40, the ratio of acid to base in equation (22) must be far from equal. By substituting the desired pH and the $pK$ into equation (22), the necessary ratio of acid to base can be determined:

\[ 7.40 = 4.76 -\log_{10} \frac{[HAc]}{[Ac^-]} \]

\[ \log_{10} \frac{[HAc]}{[Ac^-]} = -2.64 \]
A table of logarithms shows that the desired ratio of acid to base is about 1:2300, or that there must be an overwhelming excess of acetate ion present. In practice, dialysis bath solutions are prepared without any acetic acid present. The pH of these solutions is near 7.4, but the pH is very sensitive to the exact ratio of acid and base. For these reasons, acetate buffers are not an ideal choice for dialysate buffers.

Other advantages, however, outweigh their disadvantages. Acetate is not toxic. It can be readily metabolized by the body. It is, in fact, a good fuel that produces additional base as it is metabolized. For these reasons, it is widely used in dialysis bath solutions.

Since the dialysis bath solution contains almost no acetic acid, it is incapable of providing H⁺ for the patient who is alkalotic. Patients with chronic renal failure are chronically acidotic; they need to lose H⁺, and acetate is adequately suited for this purpose. For the rare patient with alkalosis, who needs to gain H⁺, acetate buffers are not adequate and special bath solutions are necessary.

**SUMMARY**

Three topics in the chemistry of hemodialysis have been presented. For those readers who may wish additional details, the following references are suggested.

**REFERENCES and NOTES**


4. Nearly all H⁺ in aqueous solution exists in hydrated form: H⁺ + H₂O → H₃O⁺. For simplicity, we have not included water as a reactant in these solutions. Further, water is a reactant in equation (7) and should be included in the denominator of equation (8). In dilute aqueous solutions, the water concentration is essentially constant and can be ignored.

5. The authors thank LINDA HOGUE for her criticism of the manuscript.