Calculations of pH for complex mixtures of acids, bases and ampholytes

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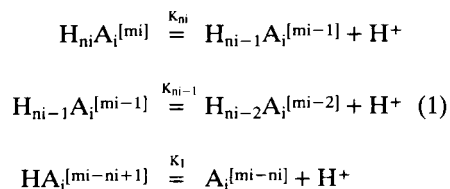*Department of Pharmacy, University of Sydney, Sydney 2006, Australia*

A general method for calculating the pH of complex mixtures of acids, bases and ampholytes is derived. Application of the method is illustrated with examples.

Calculations of pH in complex mixtures are generally carried out with the aid of simplifying assumptions which may require a considerable knowledge of the behaviour of the system. Often this intuitive approach leads to negligible errors but there are other cases, difficult to recognize, in which significant errors are involved. A general method for pH calculation has been presented by Ventura & Ando (1980). Their derivation and tabular method of evaluation are complex. They also describe a numerical procedure suitable for computer implementation but this requires calculation of polynomial coefficients, which involves much effort by the user of this method. A FORTRAN program for pH calculations is given by Martin et al (1983) but the program deals only with sample cases.

This article describes an alternative procedure for calculating the pH of complex solutions, such as buffer solutions containing a drug, without the usual simplifying assumptions. A FORTRAN program to implement the scheme is available from the author on request. All that is required of the user of this program is the basic information on pK_as, the composition of the solution and the nature of the components.

General description of acids, bases and ampholytes

All components of the system, including the solvent, are represented as ampholytes, with acids and bases interpreted as special cases. An ampholyte is taken as a collection of species in mutual equilibrium through the exchange of protons, as in the following general scheme.

$$H_{ni}A_i^{[mi]} \overset{K_{ni}}{=} H_{ni-1}A_i^{[mi-1]} + H^+$$

$$H_{ni-1}A_i^{[mi-1]} \overset{K_{ni-1}}{=} H_{ni-2}A_i^{[mi-2]} + H^+ \quad (1)$$

$$HA_i^{[mi-ni+1]} \overset{K_1}{=} A_i^{[mi-ni]} + H^+$$

The subscript i refers to a particular ampholyte (i = 1, 2, ..., N; N is the number of ampholytes). The charge on the most highly protonated species of ampholyte i is mi (including the sign; mi is negative when the charge is negative), the superscripts [mi], [mi − 1], ..., [mi − ni] represent the charges and ni, ni − 1, ... represents the number of exchangeable hydrogens for the different species which make up ampholyte i.

The special case of a polybasic acid follows on setting mi = 0, giving species $H_{ni}A_i$, $H_{ni-1}A_i^-$, ..., A_i^{ni-}. For a polyacidic base, mi = ni and the species are $H_{ni}A_i^{ni+}$, $H_{ni-1}A_i^{(ni-1)+}$, ..., A_i. The treatment of a general ampholyte therefore covers these cases, following suitable assignment of mi and ni.

For a given ampholyte species $H_jA_i^{[mi-ni+j]}$, once mi and ni are specified the charge mi − ni + j is completely determined by j. In the following the notation is simplified by omitting the charge, writing this species as H_jA_i.

In terms of concentrations the ionization constants for the equilibria in scheme (1) are defined as

$$K_{i,j} = [H_{j-1}A_i][H^+]/[H_jA_i] \quad (2)$$

From equation (2) we obtain the following

$$[HA_i] = [A_i][H^+]/K_{i,1}$$

$$[H_2A_i] = [A_i][H^+]^2/K_{i,1}K_{i,2}$$

and

$$[H_jA_i] = [A_i][H^+]^j/P_{i,j} \quad \text{for} \quad j = 1, 2, ..., ni \quad (3)$$

where

$$P_{i,j} = K_{i,1}K_{i,2}, ..., K_{i,j} \quad (4)$$

Let C_i be the total (molar) concentration of ampholyte i; that is,

$$C_i = \sum_{j=0}^{ni} [H_jA_i] \quad (5)$$

Using equation (3), this can be written

$$C_i = [A_i](1 + \sum_{j=1}^{ni} [H^+]^j/P_{i,j}) \quad (6)$$

To simplify the notation, let

$$a_{i,j} = [H_jA_j]/C_i \quad (7)$$

denote the fraction of ampholyte i in the form of the species H_jA_i, at equilibrium. Using equations (3) and (6) this becomes

$$a_{i,j} = [H^+]^j / \{P_{i,j}(1 + \sum_{j=1}^{ni} [H^+]^j/P_{i,j})\} \quad (8)$$

We now apply the electroneutrality condition. The net charge on all species present, including the counterions (not specifically referred to above), must be zero. We consider first the counterions. Let $C_{i,j}$ be the analytical (molar) concentration of species j of ampholyte i (i.e. H_jA_i). This is the concentration corresponding to the amount of H_jA_i added initially (either as a neutral species, or as a salt with a counterion). Note that $[H_jA_i]$ refers to the same species as $C_{i,j}$, but $[H_jA_i]$ refers to the equilibrium concentration, and $C_{i,j}$ to the initial concentration immediately following mixing of the components. The species H_jA_i has charge mi − ni + j, and is associated with counterions of charge ni − mi − j. Expressing charge in molar units, the total charge associated with the counterions of species H_jA_i is

$$(ni − mi − j)C_{i,j}$$

Allowing for all species of all ampholytes, the total counterion charge is

$$\sum_{i=1}^{N} \sum_{j=0}^{ni} (ni − mi − j) \, C_{i,j} \quad (9)$$

If some of the ampholytes are added as salts with other ampholytes this calculation of the counterion charge remains valid since any error due to counting non-existent positive counterions is matched by the same error, of opposite sign, arising from counting non-existent negative counterions associated with the other ampholyte of the salt.

The equilibrium concentration of species H_jA_i is $[H_jA_i]$, each molecule of H_jA_i has charge (mi − ni + j), so the total charge (in molar units) arising from species H_jA_i, i = 1, 2, ..., n, j = 0, 1, ... ni is

$$\sum_{i=1}^{N} \sum_{j=0}^{ni} (mi − ni + j) \, [H_jA_i]$$

$$= \sum_{i=1}^{N} \sum_{j=0}^{ni} (mi − ni + j) \, a_{i,j}C_i \quad (10)$$

The electroneutrality condition requires that the counterion charge, given by expression (9), be equal in magnitude and opposite in sign to the charge at equilibrium on the ampholyte species. The sum of expression (9) and the right side of equation (10) must be zero:

$$\sum_{i=1}^{N} \sum_{j=0}^{ni} (ni − mi − j) \, (C_{i,j} − a_{i,j}C_i) = 0 \quad (11)$$

In this equation, the number of ampholytes includes the solvent (unless it is inert under the prevailing conditions), which must be specified explicitly ($K_{i,j}$ for each equilibrium, and the analytical concentrations of all species). If water is the solvent, the use of equation (11) requires it to be regarded as an ampholyte comprising species H_3O^+, H_2O and OH^- (i.e. ni = 2, mi = 1) and dissociation constants are needed for the equilibria between these species.

When strong acids or bases are present equation (11) requires dissociation constants for each strong acid or base. While this is straightforward in principle there are often difficulties in obtaining reliable values for dissociation constants for strong acids or bases. When there is no doubt that a strong acid or base is completely dissociated under the prevailing conditions the following considerations lead to an alternative to equation (11) which is simpler in practice.

In equation (11), with water included as a particular ampholyte, a single term corresponds to water, which is independent of the other terms. Using the subscript w for water, taking nw = 2 and mw = 1, the term for water in equation (11) becomes

$$C_{w,0} − a_{w,0}C_w − C_{w,2} + a_{w,2}C_w$$

C_w is the concentration of water. $C_{w,0}$ is the initial concentration of $[OH^-]$, comprising that arising from water and also that arising from a completely dissociated strong base (if one is present). Thus,

$$C_{w,0} = B_0 + [OH^-]_0$$

where B_0 is the concentration of OH^- arising from completely dissociated strong bases and $[OH^-]_0$ is that arising from water. The term $a_{w,0}C_w$ is $[OH^-]$, the equilibrium concentration of OH^-. Similarly,

$$C_{w,2} = A_0 + [H^+]_0$$

where A_0 is the concentration of H^+ arising from completely dissociated acids and $[H^+]_0$ is that arising from water. The equilibrium concentration of H^+, $[H^+]$, is $a_{w,2}C_w$. Thus the term arising from water and all completely dissociated acids and bases is

$$B_0 + [OH^-]_0 − [OH^-] − A_0 − [H^+]_0 + [H^+]$$

In practical situations there is a negligible error in taking

$$K_w = [H^+][OH^-]$$

to be a constant. Thus,

$$[OH^-] = K_w/[H^+]$$

and

$$[OH^-]_0 = K_w/[H^+]_0$$

Equation (11) becomes

$$\sum_{i=1}^{N'} \sum_{j=0}^{ni} (ni - mi - j)\,(C_{i,j} - a_{i,j}C_i)$$
$$+ [H^+] - K_w/[H^+] - [H^+]_0$$
$$+ K_w/[H^+]_0 - A_0 + B_0 = 0 \quad (12)$$

In equation (12) N' is the number of ampholytes excluding water and any strong acids or bases which are present.

Calculation of pH

Calculation of the pH of a mixture of known components can be carried out using equation (11), for the general case, or equation (12) if the solvent is water. In both cases, there is only one unknown, $[H^+]$. Note that $a_{i,j}$ is a function of $[H^+]$, given by equation (8). The required value of $[H^+]$ is therefore the solution of equation (11) or (12). Ventura & Ando (1980) provide a tabular approach, and also refer to a procedure for obtaining an exact solution. The exact approach involves rearranging (their equivalent of) equation (12) to form a polynomial. When the coefficients of the polynomial form are found, standard methods of finding the roots of a general polynomial are applied. The approach adopted here is much simpler. There is no advantage in converting to a polynomial form. Instead, a numerical solution can be found by elementary methods, based directly on equations (11) or (12). This is straightforward because the pH in all practical situations can be assigned to a definite interval on the pH scale (say, 0 to 14 in the absence of any other information). The bisection (or midpoint) method (Conte & de Boor 1981) is a relatively inefficient method for general purposes, but is ideal in this application. Depending on the initial range, this method can be guaranteed to provide a solution with no more than about 12 iterations to a precision of 0·01 pH units.

As with the method of Ventura & Ando (1980) there is no ionic strength correction, which may limit the accuracy of the method. If ionic strength effects are thought to be significant, the ionization constants used in the calculation should be appropriate for the final ionic strength of the solution.

Examples

The examples which follow were those described by Ventura & Ando (1980) to illustrate their method. The results reported here were obtained using a FORTRAN program which is available on request from the author.

Example 1. Calculate pH of a solution of 0·09 M $NaHCO_3$ and 0·01 M Na_2CO_3.

Apart from water there is a single ampholyte. The most protonated form is H_2CO_3 which has zero charge (m1 = 0) and two replaceable protons (n1 = 2). The ionization constants used were those supplied by Ventura & Ando (1980). The input is summarized in Table 1.

Table 1. Data for example 1.

Ampholyte	Species	$C_{i,j}$ (M)	Equilibria	K_a*
Carbonate	A^{2-}	0·01	$A^{2-} + H^+ = HA^-$	4·8E–11
	HA^-	0·09	$A^- + H^+ = H_2A$	4·2E–7
	H_2A	0·00		

* $E = \times 10^{power}$

The program provided the value 9·37, the value reported by Ventura & Ando (1980).

Example 2. The pH is required of a solution containing 0·0216 M citric acid, 0·0216 M NaH_2PO_4, 0·0216 M barbitone, 0·0216 M boric acid and 0·0491 M NaOH.

There are four ampholytes excluding water and one strong base. We will illustrate the use of the method treating water as an ampholyte (i.e. using equation (11)) with NaOH a completely dissociated strong base. The input is listed in Table 2. The calculated pH was 5·306. Ventura & Ando (1980) calculated the value 5·30, which was the experimentally measured value.

Table 2. Data for example 2.

Ampholyte	Species	$C_{i,j}$ (M)	Equilibria	K_a
Citrate	A^{3-}	0	$A^{3-} + H^+ = HA^{2-}$	4·0E–6
	HA^{2-}	0	$HA^{2-} + H^+ = H_2A^-$	1·8E–5
	H_2A^-	0	$H_2A^- + H^+ = H_3A$	8·4E–4
	H_3A	0·0216		
Phosphate	A^{3-}	0	$A^{3-} + H^+ = HA^{2-}$	4·8E–13
	HA^{2-}	0	$HA^{2-} + H^+ = H_2A^-$	6·20E–8
	H_2A^-	0·0216	$H_2A^- + H^+ = H_3A$	7·5E–3
	H_3A	0		
Barbitone	A^-	0	$A^- + H^+ = HA$	3·&E–8
	HA	0·0216		
Borate	A^-	0	$A^- + H^+ = Ha$	5·8E–10
	Ha	0·0216		
Water	A^-	0·0491*	$A^- + H^+ = HA$	1·8E–16
	HA	55	$HA + H^+ = H_2A^+$	55
	H_2A^+	1·E–7		

* Arising from NaOH.

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