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Mathematical aspect of pH-zero point of charge relationship

Wibul Wongpoowarak and Nimit Worakul

Department of Manufacturing Pharmacy, Faculty of Pharmacy, Prince of Songkia University, Haad Yai 90112 (Thailand)

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Summary

The zero point of charge (ZPC) of antacids is useful in determining the appropriate pH of a formulation which minimizes the adsorption of ionic substances. The ZPC can be obtained approximately using a graphical method by plotting pH vs titrant volume or statistically by fitting with

$$\mathrm{pH} = P_1 + P_2 \cdot V + P_3 \cdot V^2 + P_4 \cdot V^3 + P_5 \cdot V^4 + P_6 \cdot \sqrt{\mu} + P_7 \cdot V \cdot \sqrt{\mu}$$

where V is the volume of acid or base as titrant and μ represents ionic strength or any unit directly proportional to the ionic strength.

The most important problem usually encountered in the formulation of aluminum hydroxide gel preparations is microbial contamination. Even at a rather high concentration of preservative, this problem remains a crucial factor due to the adsorption of preservative by the aluminum hydroxide gel. The process of adsorption is mainly due to the electrostatic force arising from pH-dependent surface charge. It can be reduced significantly by adjusting the pH of the preparation to the pH value at zero point of charge (Feldcamp et al., 1981; Shah et al., 1982).

The method of titration is normally used to determine the zero point of charge (ZPC). This procedure is based on the principle that changes in the ionic strength produced by the addition of electrolyte, such as KCl, would have no effect on proton adsorption or release by the gel when the gel surface charge is zero. Thus, the titration curves obtained at various ionic strengths should intersect at a common point, the so-called ZPC (Feldcamp et al., 1981; Shah et al., 1982). The antacid is titrated with a mineral acid or mineral base such as HCl or KOH at different values of the volume or milliequivalent (meq.) of titrant. The pH-meq. or pH-ml titrant profile at various ionic strengths could intersect at the same point, according to the Debye-Hückel concept of ionic strength, the so-called zero-point of charge. Normally, this point is determined via a graphical method which may be difficult to interpret in the case where all the lines do not intersect at exactly the same point. However, the more reliable ZPC

Correspondence: W. Wongpoowarak, Department of Manufacturing Pharmacy, Faculty of Pharmacy, Prince of Songkia University, Haad Yai 90112, Thailand.

TABLE 1

Effect of HCl, KOH and electrolyte on pH of aluminum hydroxide gel

Volume (ml)		pH	
Acid	KCl solution	Measured	Predicted
0	0	7.99	7.95
0	10	7.80	7.78
0	20	7.74	7.70
1	0	7.57	7.58
1	10	7.42	7.45
1	20	7.40	7.40
2	0	7.18	7.19
2	10	7.11	7.10
2	20	7.08	7.07
3	0	6.86	6.84
3	10	6.78	6.79
3	20	6.76	6.78
4	0	6.60	6.56
4	10	6.54	6.56
4	20	6.53	6.56
4.2	0	6.54	6.52
4.2	10	6.52	6.52
4.2	20	6.51	6.52
4.4	0	6.46	6.47
4.4	10	6.48	6.48
4.4	20	6.49	6.49
4.6	0	6.43	6.43
4.6	10	6.45	6.45
4.6	20	6.48	6.46
4.8	0	6.39	6.39
4.8	10	6.42	6.42
4.8	20	6.46	6.44
5	0	6.32	6.36
5	10	6.40	6.40
5	20	6.43	6.41
−0.2	0	8.03	8.01
−0.2	10	7.83	7.83
−0.2	20	7.76	7.76
−0.4	0	8.06	8.06
−0.4	10	7.86	7.88
−0.4	20	7.79	7.80
−0.6	0	8.10	8.12
−0.6	10	7.90	7.92
−0.6	20	7.82	7.84
−0.8	0	8.14	8.16
−0.8	10	7.94	7.96
−0.8	20	7.86	7.87
−1	0	8.19	8.20
−1	10	7.98	7.98
−1	20	7.90	7.90
−1.2	0	8.22	8.22
−1.2	10	8.02	8.00
−1.2	20	7.94	7.91

The pH was predicted from Eqn 11. Volume of acid is negative in the case of KOH used as titrant with HCl it is positive.

can be evaluated numerically by fitting the pH-volume titrant profiles at varying ionic strengths to an empirical equation which can be used to represent this phenomenon.

Let

$$\mathrm{pH} = f(V) + g(V, \mu) \tag{1}$$

$$\mathrm{pH}_{\mu=0} = f(V) \tag{2}$$

where V denotes volume or meq. of titrant, μ is ionic strength or any measurement unit which is directly proportional to the ionic strength, such as the volume of the electrolyte solution, $f(\ )$ represents the predictor function of pH due to the effect of titrant and $g(\ )$ is the correction function for Eqn 1.

V can be regarded as having a negative value when KOH (base) is employed as titrant, with a positive value in the case of HCl (acid).

At the ZPC, let the volume of titrant used be V_c, at which

$$g(V_c, \mu) = 0 \tag{3}$$

This expression is equivalent to Eqn 2.

The empirical model used to fit Eqn 2 is a polynomial function. The degree of this polynomial function should be greater than 3 to describe the sigmoidal portion of the graph, and not excessively high in order to avoid wiggle phenomena which are commonly found in polynomial functions of high degree.

In this case, the maximum degree of the polynomial function for $f(V)$ is arbitrarily set to 4, hence,

$$\mathrm{pH} = P_1 + P_2 \cdot V + P_3 \cdot V^2 + P_4 \cdot V^3 + P_5 \cdot V^4 \tag{4}$$

According to the Debye-Hückel concept, the deviation in pH as a result of different ionic strengths varies approximately with $\sqrt{\mu}$,

$$g(V, \mu) = h(V) \cdot \sqrt{\mu} \tag{5}$$

From Eqns 3 and 5, and preliminary study,

$$h(V)_{V=V_c} = 0;\ h(V)_{V<V_c} > 0;\ h(V)_{V>V_c} < 0 \tag{6}$$

The empirical form of $h(V)$ which satisfies Eqn 6 is

$$h(V) = k(V_c - V)^{2n+1}; \quad n = 0.1,2,\ldots \tag{7}$$

The simplest form of Eqn 7 is at $n = 0$.

Hence, we obtain the simplest form of the empirical model which is expressed as follows:

$$\begin{aligned} \mathrm{pH} = {} & P_1 + P_2 \cdot V + P_3 \cdot V^2 + P_4 \cdot V^3 + P_5 \cdot V^4 \\ & + P_6 \cdot \sqrt{\mu} + P_7 \cdot V \cdot \sqrt{\mu} \end{aligned} \tag{8}$$

At the ZPC, V_c can be solved from Eqns 3, 5 and 7;

$$V_c = -(P_6/P_7) \tag{9}$$

and

$$\mathrm{pH}_{Vc} = P_1 + P_2 \cdot V_c + P_3 \cdot V_c^2 + P_4 \cdot V_c^3 + P_5 \cdot V_c^4 \tag{10}$$

The V_c, pH at V_c can readily be determined if $P_1 \ldots P_7$ are known. Normally, the treatment of the data can be carried out through any standard statistical package or by a computer program designed for this particular purpose by using the matrix equation to solve for least-square regression (Mathews, 1987). The equation can be modified by employing a polynomial function of higher degree in Eqn 4 or a different model for $h(V)$ in Eqn 7.

With the model data (Worakul, 1991; see Table 1), Eqn 8 is satisfactorily applicable, the errors of prediction falling close to the pH meter uncertainty (maximum error of prediction = 0.04 pH units). The ionic strength here (μ) can also be represented by the volume of electrolyte (KCl) without any marked difference in the pH value at the ZPC.

$$\begin{aligned} \mathrm{pH} = {} & 7.945556 - 0.3251599 \cdot V - 0.05642412 \cdot V^2 \\ & + 0.01756487 \cdot V^3 \\ & - 0.001192486 \cdot V^4 \\ & - 0.05392381 \cdot \sqrt{\mu} + 0.01316889 \cdot V \cdot \sqrt{\mu} \end{aligned} \tag{11}$$

In this case, the volume of HCl (4.10 ml) must be used in order to ascertain the ZPC (at pH 6.54).

This empirical model allows the ZPC of antacid to be evaluated statistically with greater reliability of the results being achieved. The data points may be reduced or need not be measured with particular attention at the suspected point, and yet a similar result will be obtained.

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