Application Note

Determination of cimetidine by titration with acetic acid as solvent

Industry	:	Pharmaceutical
Instrument	:	Automatic potentiometric titrator
Measurement method	:	Potentiometric titration / Neutralization titration
Standards	:	Japanese Pharmacopoeia

1. Scope

Cimetidine is one of the pharmaceutical listed in the Japanese Pharmacopoeia. This application introduces an example of quantifying cimetidine based on the Japanese Pharmacopoeia.

2. Precautions

In this titration, acetic acid is used as the solvent.Contamination of the test solution with water causes the titration curve to become unstable and cause errors. Use either of the following internal liquid to avoid water contamination.

(A) 1 mol / L lithium chloride (acetic acid solution)
(B) Saturated sodium perchlorate (acetic acid solution)

The internal liquid of (A) is sold by us. Please contact us if you have a request. The internal liquid of (B) needs to be prepared by the customer. After saturating anhydrous sodium perchlorate in acetic acid, use the supernatant liquid.

3. Post-measurement procedure

Seal the refill port for internal liquid of reference electrode by rubber plug so that internal liquid is prevented from leaking out and concentrating.
When the glass electrode is stored in a dry state, the performance is rapidly reduced. Store the glass electrode as follows.

- Short-term storage (less than one month): Immersion in pure water.
- Long-term storage (more than one month): Immersion in a mixed solution of pH 4 standard solution and 3.3mol/L KCl aq in a volume ratio of 1: 1

4. Apparatus

- Automatic potentiometric titrator (preamplifier : STD)
- pH glass electrode
- Reference electrode (Double junction type)
(inner liquid : 1 mol / L lithium chloride (acetic acid solution))

5. Reagents

- 0.1mol/L Perchloric acid (acetic acid solution)
- Acetic acid

6. Procedure

1) About 0.24 g of the sample was precisely weighed in a beaker.
2) 75 mL of acetic acid was added to the beaker to completely dissolve the sample.
3) The sample was titrated with 0.1 mol / L perchloric acid (acetic acid solution).
4) The blank test was performed in the same way, and the titration amount was corrected.

7. Calculation

Purity of cimetidine (%) = (EP1-BL1)×TF×C1×K1 / S

EP1	・・・Titration amount of sample (mL)	
BL1	・・・Titration amount of blank test	＝0.0126
TF	・・・Factor of titrant	＝0.9763
C1	・・・Concentration conversion coefficient	＝25.23mg/mL
K1	・・・Unit conversion coefficient	＝0.1
S	・・・Quantity of sample (g)	

8. Example

-Titration parameter-

＜Titr. Mode＞ : Auto Intermit
＜Titr. Form＞ : EP Stop

＜Titr. Para.＞

Max. Volume	: 20 (mL)
Channel/Unit(Ctrl.)	: Ch1, mV
Channel/Unit(Ref.)	: Off
pH Polarity	: Standard
Titr. Type Check	: No Check
Direction	: Negative
Wait Time	: 10 (s)
Dose Mode	: None

＜Ctrl. Para.＞

Number of EP	: 1
End Sense	: Auto
Gain	: 1
Data Sampling	: Auto
Ctrl. Speed	: Standard
Other Ctrl.	: Standard
Auto Int. Mode	: Standard
Stirrer Speed	: 4

(The measurement parameter and the titration curve are an example of our automatic potentiometric titrator. For other models, parameter item may be different or other parameter item may be added.)

—Titration curve—

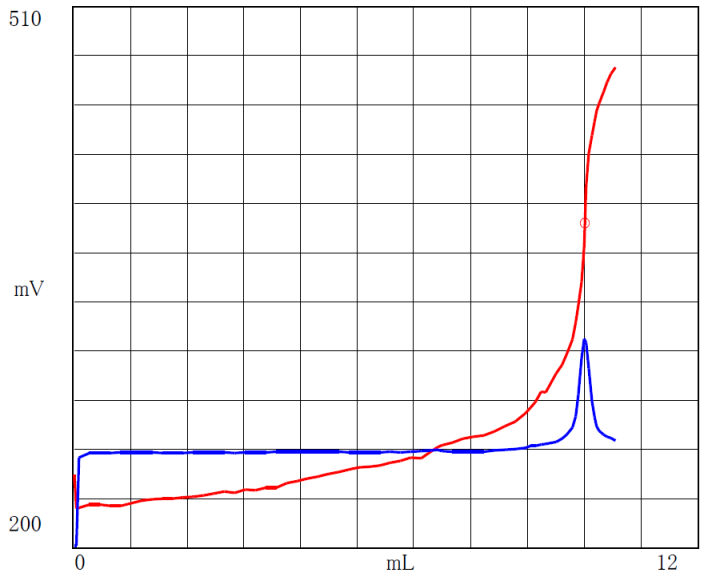

Table1 Measurement result

	Sample (g)	Titration amount (mL)	quantitative value (%)
1	0.2442	9.9331	100.07
2	0.2420	9.8440	100.07
3	0.2438	9.9052	99.95
Mean	-	-	100.03
SD	-	-	0.07
RSD(%)	-	-	0.07

9. Summary

The test samples were measured three times, and the results of them showed a good repeatability. The measurement results were within the range of quantitative values (99.0 to 101.0%) in the Japanese Pharmacopoeia.

10. For your information

Weak bases with a pK_b of 7 or more are difficult to quantify as potential jump at the end point is small in aqueous solution. Some pharmaceuticals are also poorly soluble in water. Pharmaceuticals that are poorly soluble in water can't be titrated in aqueous solutions. Non-aqueous titration with acetic acid solves these problems. Acetic acid has high proton donor ability. As a result, weak base compounds behave as strong bases in acetic acid. The potential jump at the end point of titration is large by using acetic acid as a solvent. Therefore, it is possible to quantify weak bases. For this reason, non-aqueous titration is defined as a quantitative method for many pharmaceuticals in the Japanese Pharmacopoeia.