

Application Note

Moisture of Folic Acid

Industry	:	Pharmaceutical
Instrument	:	Karl Fischer Moisture Titrator
Measurement method	:	Coulometric titration/ Direct method
Standards	:	The Japanese Pharmacopoeia 17th edition

1. Scope

In the Japanese Pharmacopoeia it is stipulated that the water content of folic acid should be measured by Karl Fischer's coulometric titration method. The acceptance criterion is that the moisture concentration is 8.5% or less.

In this application, we introduce an example in which the water concentration of folic acid is measured by the coulometric titration method.

2. Precautions

- In order to suppress the influence of the moisture of the outside air, please measure in indoor room with air conditioning equipment.
- If possible, please use an electronic balance that can measure up to 0.01 mg digits.

3. Post-measurement procedure

After draining the anolyte and catholyte, wash the titration flask, electrolytic electrode and platinum electrode with methanol.

4. Apparatus

Main unit : Karl Fischer moisture titration coulometric system
 Electrode : Electrolysis electrode, Twin platinum electrode

5. Reagents

Anolyte : KEM AQUA Anolyte AGE
 Catholyte : KEM AQUA Catholyte CGE

6. Procedure

- Preparation -

- 1) Fill approximately 100 mL of anolyte solution into titration flask.
- 2) Fill approximately 5 mL of catholyte in electrolytic electrode.
- 3) Attach the “sampling set”[※] to the titration flask.
- 4) Perform preliminary titration to make the inside of the titration cell anhydrous.

- Measurement -

- 1) Collect a sample in a cup attached to the “sampling set”.
- 2) Set the cup in a “sampling set” and attach the cover.
- 3) Pull the lever of the “sampling set” and insert the cup into the titration cell and perform the measurement.
- 4) In the same procedure, put an empty cup into the titration flask and measure it, and use it as a blank test value.

※The “sampling set” can be used for putting the small amount of sample in the titration cell of the Karl Fischer titrator

7. Calculation

$$\text{Moisture (\%)} = F \times (\text{Moisture} / (\text{Wt1} - \text{Wt2})) \times k$$

F: Compensation coefficient(1)

Wt1 : Sample+ Syringe weight(g)

Wt2 : Empty syringe(g)

k : Unit conversion coefficient(0.0001)

Moisture : (Data – Drift × t – Blank) (μg)

Data : Total moisture(μg)

Drift : Drift level(μg/s)

t : Measuring time(s)

Blank : Blanklevel(32.8 μg)

8. Example

-Titration parameter-

<Titr.Para>

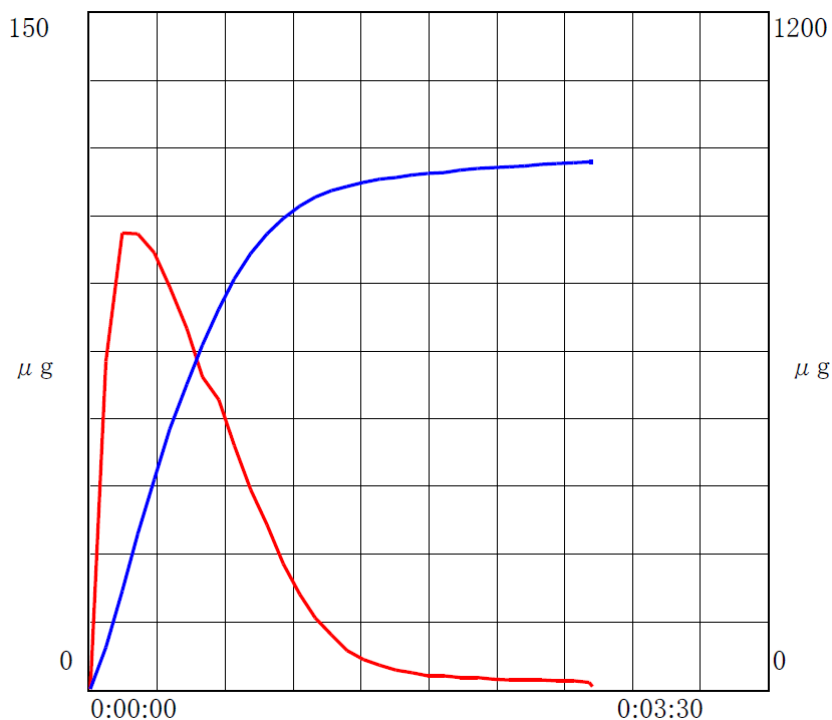
Titration mode	: H ₂ O
t(stir)	: 0s
t(wait)	: 15s
t(max)	: 0 s
Drift stop	: Rel.
Rel.	: 0.1μg/s

<Ctrl.Para>

Cell type	: 2-comp.
Stable	: 0.10μg/s
Control gain	: 5.0
Electrolysis speed	: Standard
End level	: 200mV
Start mode	: Manual
Data sampling time	: 5s
Stirrer speed	: 3

(The measurement parameter and the titration curve are an example.)

-Titration curve and results-



	Sample size(g)	moisture(μg) [*]	Concentration of water content (%)
1	0.0104	870.0	8.37
2	0.0102	861.1	8.44
3	0.0105	843.5	8.03
AVE	-	-	8.28
SD	-	-	0.22
RSD(%)	-	-	2.65

※ The moisture is the value obtained by subtracting the blank level 32.8 μg .

9. Summary

Repeatability was less than 3% in RSD value, so good accuracy was obtained. In addition, the results satisfied the acceptance criteria prescribed in the Japanese Pharmacopoeia.

The “sampling set” used in this application has the advantage that it can be sampled and introduced easily even with a small amount of sample, and the sample does not adhere to the wall surface of the flask.