

**Water  
contents****Drugs and Medicines – KF Coulometry  
Thiamine Chloride Hydrochloride and Folic Acid****1. Abstract**

Water contents of drugs and medicines could be determined by Karl Fischer coulometric titrator. In coulometric titration, iodine of Karl Fischer reagent is generated by electrolysis and generated iodine quantitatively reacts with water. Reaction formula is described below.



When the moisture content is relatively high at the % level, the amount of sample added is as small as a few 10 mg. If the sample is in powder form, taking and adding samples with an “ultra-micro solid sampler” makes measurement easy and accurate. An example for water contents measurements of thiamine chloride hydrochloride and folic acid performed by with ultra-micro solid sampler are introduced here. The measurement method was determined with reference to *Japanese Pharmacopoeia*.

Reference

1) Japanese Pharmacopoeia Seventeenth Edition

**2. Apparatus and Reagents**

## (1) Apparatus

Titration : Hiranuma Karl Fischer Coulometric titrator AQ-series  
Electrolytic cell : Standard Cell without drain valve (P/N E324017-1)

## (2) Reagents

Anode solution : HYDRANAL Coulomat AG (Honeywell)  
Cathode solution : HYDRANAL Coulomat CG (Honeywell)

(3) Sampling tool : Ultra-micro solid sampler (P/N E730016-A, Fig.2.1)



Fig.2.1 Ultra-micro solid sampler

### 3. Procedure

- (1) Fill 100 mL of anode solution and one ampoule of cathode solution into the electrolytic cell as shown in Fig.3.1.
- (2) Set the ultra-micro solid sampler on the lid of cell as shown in Fig.3.2.
- (3) Start blanking to attain stable background.
- (4) Take sample into the capsule and accurately weigh it.
- (5) Set the capsule on the sampler as pictured in the Fig.3.3.
- (6) Pull the plate of sampler to introduce capsule into the cell.
- (7) Start titration. Measurement parameter is shown in Table 4.1.
- (8) Set sample weight to sample size.

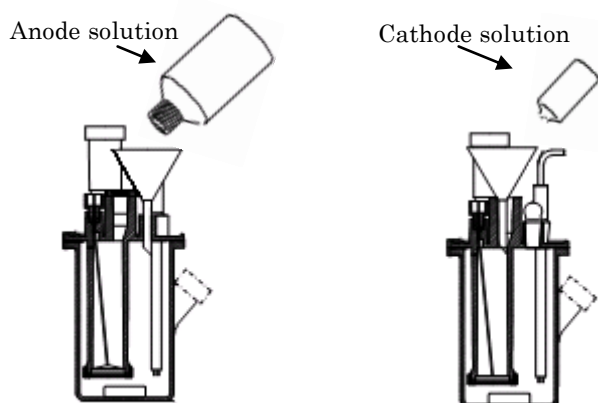


Fig.3.1. Preparation of the reagents.



Fig.3.2 Setting of ultra-micro solid sampler

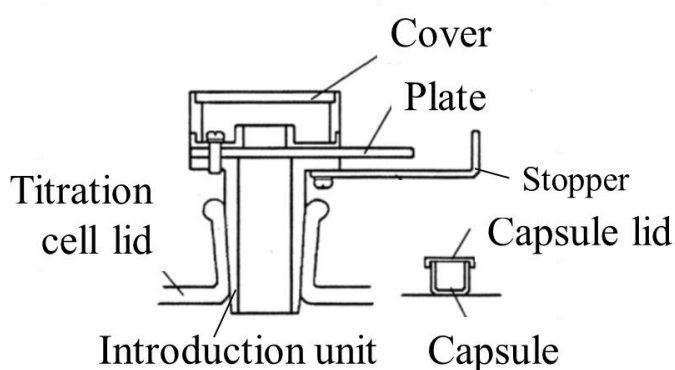


Fig.3.3. Introduction of sample.

## 4. Parameters and results

Table 4.1. Parameters

Condition File	
Cal Mode	0:Sample weight (net) $X=(H_2O-BLANK)/SIZE$
Interval Time	30 sec
Current	MEDIUM
S.Timer	10 min
Blank Value	0 ug
Unit Mode	AUTO
Auto Interval	0 g
Minimum Count	5 ug
Back Ground	ON
Sample Size Input	Every Time
Cell Type	Standard

Table 4.2. Results of water content measurement in drugs and medicines

Sample	Sample size (mg)	Water (µg)	Water content (%)	Statistics result	Remark
Thiamine Chloride Hydrochloride	33.2	1005.4	3.0283	Avg. 3.0245 %	insoluble
	30.3	912.7	3.0122	SD 0.0109 %	
	32.4	982.7	3.0330	RSD 0.4 %	
Folic acid	12.5	814.9	7.8356	Avg. 7.7329 %	insoluble
	15.0	962.9	7.7032	SD 0.0915 %	
	11.5	880.9	7.6600	RSD 1.2 %	

## 5. Note

- (1) Sampler, capsule and the other tools should be dried up well before use.
- (2) After adding 10 to 20 capsules to the cell, open the cell lid and remove the capsule. Capsules can be washed and reused.
- (3) To measure 100 µg or less water detection, make sure stability of blanking. Low and stable background value is important factor for trace level of water measurement.

Keywords : Karl Fischer, Coulometric titration, Pharmacopeia, Solid