

HIRANUMA APPLICATION DATA	Karl Fischer Titrator	Data No.	KF 10V	Apr. 19, 2018
Water contents	Drugs and Medicines – KF Volumetry Direct-Injection Propylene glycol and Glycerin			

1. Abstract

Water contents of drugs and medicines could be determined by Karl Fischer volumetric titrator. In volumetric titration, titrant have a titer which means the capacity to react with water per 1 mL of titrant. Factor is pre-determined before sample measurement and water content of sample is calculated from consumed titrant volume within sample measurement.

When the sample is liquid, generally sample is measured by direct injection into the cell. Dehydrated methanol is used for titration solvent. The titration solvent may change to a composition suitable for dissolving the sample.

Examples for water contents measurements of propylene glycol and glycerin performed by direct injection method are introduced here. The measurement method was determined with reference to *Japanese Pharmacopeia*.

Reference

1) Japanese Pharmacopoeia Seventeenth Edition

2. Apparatus and Reagents

(1) Apparatus

Titrator	:	Hiranuma Karl Fischer Volumetric titrator	AQV-series
Titration cell	:	Standard Cell	

(2) Reagents

Titrant	:	HYDRANAL Composite 5 (Honeywell)
Titration solvent	:	HYDRANAL Methanol (Honeywell)

3. Procedure

- (1) Fill 50 mL of titration solvent into the titration cell as shown in Fig.3.1.
- (2) Start blanking to attain stable background.
- (3) Wash the syringe with sample.
- (4) Draw the sample into syringe and then weigh the syringe.
- (5) Inject sample from rubber septum of titration cell as shown in Fig.3.2.
- (6) Start titration. Measurement parameter is shown in Table 4.1.
- (7) Weigh the syringe again and then set the difference of weight to sample size.

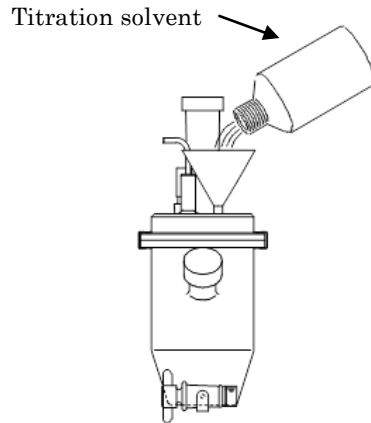
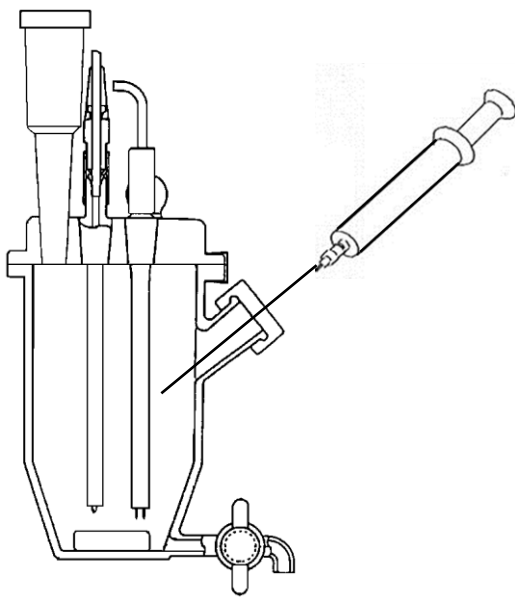


Fig.3.1 Preparation of the reagents



Note

- (1) Do not touch the tip of needle to titration solvent.
- (2) When injecting, set the tip of needle as below figure.



- (3) Before pulling out the needle, draw a little air to prevent dripping of sample.

Fig.3.2 Injection of sample

4. Parameters and results

Table 4.1 Parameters

Condition File	
Cal Mode	0:Sample weight (net) $X=(H-b)\times F\times 1000/SIZE$
Interval Time	30 sec
Max Volume	20 mL
Min Feed Vol.	0.01 mL
S.Timer	0 min
KF Factor	5.7614 mg/mL
KF Buret No.	1
KF Speed(OUT)	12 mL/min
KF Speed(IN)	24 mL/min
Back Ground	OFF
Sample Size Input	Every Time
Blank Value	0 mL
Unit Mode	AUTO
E.P Detection	mV
Solvent	S,O,CE
C.P Level	150 mV
E.P Level	1
Auto Interval	0 g

Table 4.2 Results of water content measurement in drugs and medicines

Sample	Sample size (g)	Titrant volume (mL)	Water (mg)	Water content (ppm)	Statistics result		Remark
Propylene glycol	2.0482	0.30	1.728	843.7	Avg.	860.9 ppm	KF Factor
	2.0517	0.31	1.786	870.5	SD	14.9 ppm	5.7614 mg/mL
	1.9240	0.29	1.671	868.5	RSD	1.73 %	
Glycerin	6.9553	1.27	7.259	1043.7	Avg.	1047.6 ppm	KF Factor
	7.0613	1.29	7.374	1044.3	SD	6.3 ppm	5.7160 mg/mL
	7.1525	1.32	7.545	1054.9	RSD	0.60 %	

5. Note

- (1) Sampling tools should be dried up well before use.
- (2) Purge and fill the titrant homogeneously into the buret.
- (3) Organic solvents which have relatively high volume expansion coefficient are used as a constituent of titrant. For accurate measurement, factor titration and sample measurement should be performed at the same room temperature as much as possible.

Keywords : Karl Fischer, Volumetric titration, Pharmacopeia