

## Application Note

# Determination of Acrinol Monohydrate by Titration with Acetic Acid / Acetic Anhydride as Solvent

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

## 1. Scope

Acrinol monohydrate is one of the pharmaceuticals listed in the Japanese Pharmacopoeia. This application introduces an example of the determination of acrinol monohydrate based on Japanese Pharmacopoeia.

The Japanese Pharmacopoeia stipulates, “Acrinol Hydrate contains not less than 98.5 % and not more than 101.0 % of acrinol, calculated on the anhydrous basis.” Accordingly, the moisture content must be measured separately by the Karl Fischer method.

## 2. Precautions

The sample is not easily dissolved in the solvent, so stir it thoroughly, and do not start the measurements until the sample is completely dissolved.

In this measurement, water contamination causes an error. In order to avoid water contamination, use one of the following electrolyte for the reference electrode.

- (1) 1mol / L Lithium chloride solution in acetic acid
- (2) Saturated sodium perchlorate solution in acetic acid

Electrolyte (1) is available from KEM, so contact us if you would like to order it. Electrolyte (2) must be prepared by the operator. When preparing this solution, saturate acetic acid with anhydrous sodium perchlorate, and use the supernatant liquid.

## 3. Post-measurement procedure

Seal the refill port for internal liquid of reference electrode by rubber septum so that electrolyte is prevented from leaking out or concentrating, and store the electrode.

The performance of the glass electrode quickly degrades if it is stored while dry. The following storage methods are recommended.

- Short-term storage (less than one month): Store it immersed in pure water.
- Long-term storage (one month or longer): Store it immersed in a 1:1 volume ratio mixture of a standard solution of pH4 and a 3.3 mol/L KCl solution.

## 4. Apparatus

Main unit	:	Automatic potentiometric titrator (preamplifier : STD)
Electrode	:	Glass electrode Double junction reference electrode type (Electrolyte: 1mol/L Lithium chloride in acetic acid)

## 5. Reagents

Titrant : 0.1mol / L Perchloric acid solution in acetic acid  
 Solvent : Formic acid (purity 98-100%),  
 A mixture of acetic anhydride and acetic acid in a volume ratio of 1:1

## 6. Procedure

-Measurement-

- 1) Collect about 0.27 g of sample into a beaker, and measure the mass.
- 2) Add 5 mL of Formic acid, dissolve the sample
- 3) Add 60 mL of a mixture of acetic anhydride and acetic acid. Immediately titrate with a 0.1 mol/L perchloric acid acetic acid solution.
- 4) Using the same procedure, perform a blank test, and correct the titration volume.

## 7. Calculation

Purity of Acrinol monohydrate (%) =  $(EP1 - BL1) \times TF \times C1 \times K1 / (S \times ((100 - SMW) / 100))$

EP1	:	Titration volume (mL)
BL1	:	Titration volume (mL) of Blank test = 0.04993
TF	:	Factor of Titrant = 1.04695 *1
C1	:	Concentration conversion coefficient= 34.34mg/mL
K1	:	Unit Conversion coefficient= 0.1
S	:	Sample size (g)
SMW	:	Moisture content of sample = 5.1999% *2

\*1 This factor is calculated by using potassium hydrogen phthalate, the standard substance for volumetric analysis, as the standard. Refer to the Japanese Pharmacopoeia for details on standardization procedures.

\*2 The moisture content of the sample is measured separately with a Karl Fischer moisture meter for volumetric titration.

Refer to the Japanese Pharmacopoeia for details on the moisture content measurement method.

In addition, refer to KEM Application Note APKF-0153.

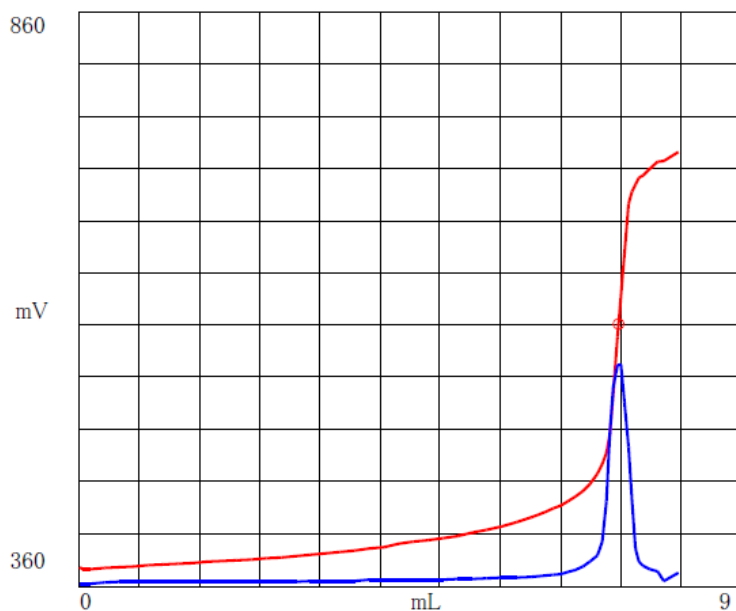
## 8. Example

— Parameter —

<u>&lt;Titr. Mode&gt;</u>	: Auto Intermitt	<u>&lt;Ctrl. Para.&gt;</u>	
<u>&lt;Titr. Form&gt;</u>	: EP Stop	End Point No.	: 1
		Gain	: 1
<u>&lt;Titr. Para.&gt;</u>		End Sense (dE/dmL)	: Auto
Bullet No.	: 1	Data Sampling	: Auto
Max Volume	: 20 (mL)	Ctrl. Speed	: Standard
Channel/Unit (Ctrl.)	: Ch1, mV	Other Control	: Standard
Channel/Unit (Ref.)	: Off	Stirrer Speed	: 4
pH Polarity	: Standard		
Titr. Type Check	: None		
Direction	: Auto		
Wait Time	: 0 (s)		
Dose Mode	: None		

(The settings above are just one example. They may vary depending on the model.)

— Example of Titration curve —



— Measurement results —

Table 1 Measurement results of Acrinol monohydrate

	Sample (g)	Titration volume (mL)	Time (h:m:s)	Purity (%)
1	0.2744	7.4306	0:04:40	100.76
2	0.2776	7.3831	0:04:04	100.18
3	0.2751	7.3435	0:04:26	100.54
Mean				100.49
SD				0.29
RSD (%)				0.29

9. Summary

Excellent accuracy was obtained with a relative standard deviation (RSD) of less than 1 %. In addition, the results obtained satisfied the requirements (98.5 to 101.0 %) stipulated in the Japanese Pharmacopoeia.

Acrinol monohydrate can be determined using an automatic potentiometric titrator from KEM.