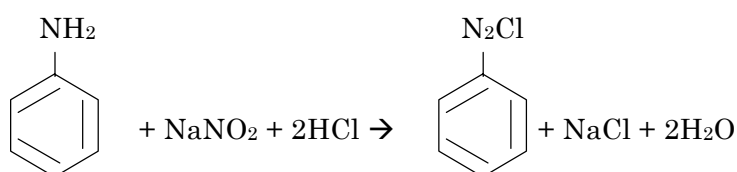


AQUACOUNTER Application Sheet	COM series	DATA No. B9	1st edition
Pharmaceuticals	Evaluation of titer of sodium nitrite titrant with sulfamic acid		

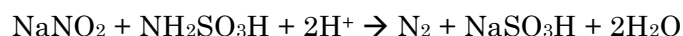
1. Measurement outline

The method for quantifying medical products by sodium nitrite using the diazotization reaction of aromatic primary amine with nitrite salt is stipulated in Japanese Pharmacopoeia and is utilized widely for measurement of purity of medical products.

This measurement is also called diazotization titration, and aromatic primary amine reacts with sodium nitrite as follows:



In addition, sodium nitrite reacts with sulfamic acid under acidic conditions with hydrochloric acid as follows:



This reaction is a type of oxidation-reduction reaction in which sodium nitrite oxidized the amino group (NH_2) to nitrogen.

Since sulfamic acid can be used as the primary standard in this reaction, it is used for evaluation of sodium nitrite titrant. However, this reaction has a slow reaction speed and caution is required in setting its method of end point detection as well as measurement conditions. This section introduces an example of evaluating sodium nitrite titrant with sulfamic acid.

2. Reagents and Electrodes

(1) Reagents	Titrant	0.1mol/L sodium nitrite titrant
	Standard sulfamic acid reagent(certified by National Institute of Technology and Evaluation)	
	Hydrochloric acid 10mL for 1 measurement	
(2) Electrodes	Twin platinum electrode TPT-351	*P-2000 standard accessory

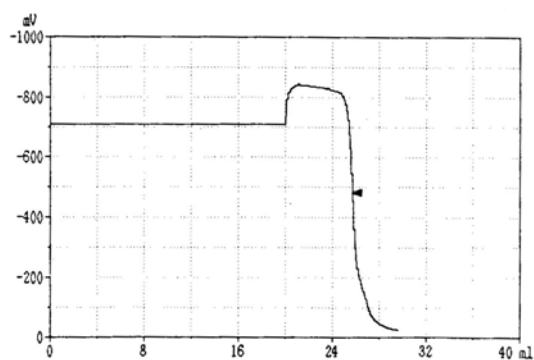
3. Measurement conditions example (for COM-1600P w/ Polarization titration unit)

Master File No.1	
Condition file: 1	
Method	AUTO
Amp No.	2
Buret No.	1
Meas Unit	mV
S-Timer	300 sec
CP	20 mL
DP	0 mL
Direction	N/A
End Sens	500
Over mL	0 mL
Max Vol	30 mL
Mode No.	21
Unit	Fact 2
Blank	0
Factor	0
Molarity	0.1
K	97.09
Formula	$S \times 1000 / (K \times M \times (D - B))$

Mode No.21	
Pre Int	10 sec
Del K	0
Del Sens	0 mV
Int Time	10 sec
Int Sens	3 mV
Brt Speed	2
Pulse	80

Polarization current: 1μA

4. Measurement example



Sample measurement results

Sample No.	Sample volume (g)	Titration value (mL)	Titer
1	0.2564	26.212	1.008
2	0.2509	25.670	1.007
3	0.2536	25.947	1.007
4	0.2572	26.279	1.008
5	0.2603	26.613	1.007
6	0.2541	25.957	1.008

<u>Avg.</u>	<u>1.008</u>
<u>Std. Dev.</u>	<u>0.001</u>
<u>C.V.</u>	<u>0.054 %</u>

5. Outline

In diazotization titration, favorable results can be obtained by noting the following points:

- (1) Since the reaction speed is low, titration shall be conducted successively until it is near the end point in advance to shorten the measurement period. When it is near the end point, titration shall be conducted by repeating the fixed volume of dropping and fixed waiting period with a slow speed.
- (2) Since this reaction is slow, condition in which sodium nitrite is excessive is repeated in the titrated solution at each dropping of the titrant. During this period, sodium nitrite is exposed to a strongly acidic condition and may become partly evaporated. Thus it is desired that the solution is kept at 15°C or lower. However, the reaction speed is further reduced if it is cooled too much. It is said that the appropriate temperature is 5– 15°C.
- (3) Though they cannot be used as the primary standard, sulfanilamide ($\text{H}_2\text{NC}_6\text{H}_4\text{SO}_2\text{NH}_2$) or sulfanilic acid ($\text{H}_2\text{NC}_5\text{H}_4\cdot\text{SO}_3\text{H}$) can be used as alternatives to sodium nitrite in daily evaluation since they have faster reaction speeds. Amidosulfuric acid can also be used, but its reaction is slow and requires caution.
- (4) Potassium bromide is said to catalyze diazotization, and Japanese Pharmacopoeia stipulates so that titration is conducted with addition of 10mL potassium bromide solution (3→10). Furthermore, the concentration of hydrochloric acid for titration affects the reaction speed and it is desired that the concentration of hydrochloric acid for the titrated solution be 1 – 3mol/L.
- (5) Though the relationship with the sample when polarization titration is used is valid for samples with slow reaction, it is not effective for samples with fast reaction (sulfanilamide) and the titration curve tends to become unclear.

Key words

Medical product, diazotization titration, sulfamic acid, sodium nitrite, measurement unit for polarization titration

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