Analysis of Tranexamic Acid According to the Japanese Pharmacopoeia

Tranexamic acid is an artificial amino acid used as a hemostatic or anti-inflammatory drug because it inhibits the activity of plasmin, which dissolves blood clots.

It also inhibits melanin production and is effective in improving and preventing sun spots and freckles. It may be contained in drugs taken by mouth or in toilets.

In the 17th edition of the Japanese Pharmacopoeia (JP17), the HPLC method is adopted in the test for multiple tranexamic acids. The HPLC guidelines have defined the system suitability items specified for each system. In this application an HPLC analysis based on a JP17 method was evaluated and excellent results were obtained.

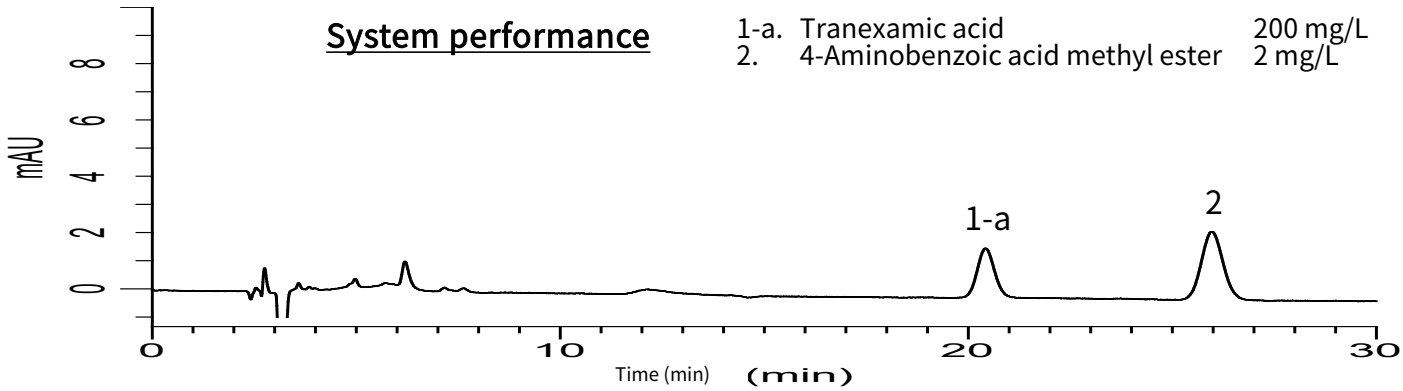
(M. Kobayashi)

Tranexamic Acid Determination

*Adjust the flow rate so that the retention time of tranexamic acid is approx. 20 minutes.

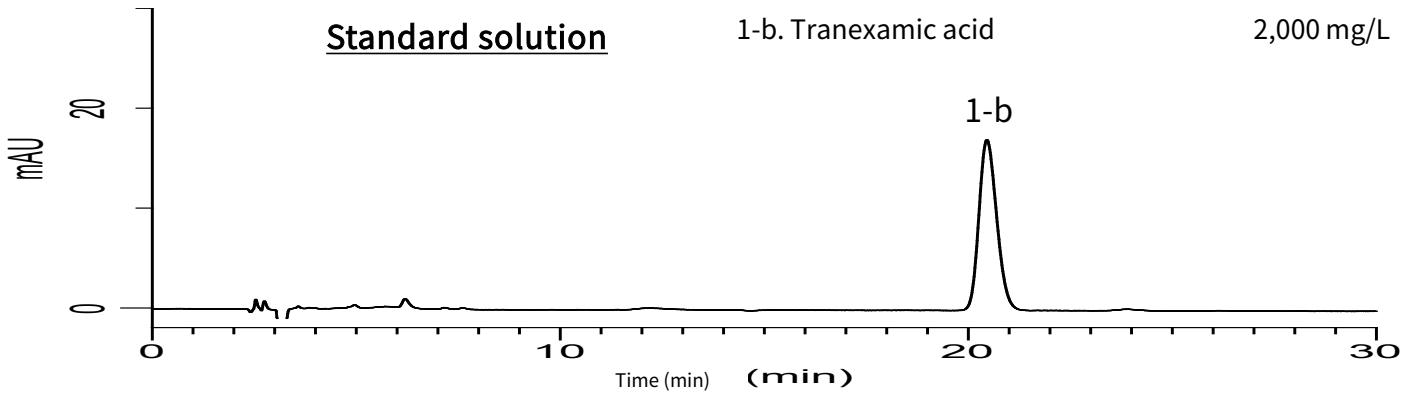
System performance

1-a. Tranexamic acid 200 mg/L
2. 4-Aminobenzoic acid methyl ester 2 mg/L



Standard solution

1-b. Tranexamic acid 2,000 mg/L



HPLC conditions

Column	: InertSustain AQ-C18 (5 µm, 250 x 6.0 mm I.D.)
Eluent	: A) Phosphate buffer *1 B) CH_3OH A/B = 60/40, v/v
Temperature	: 25 ˚C
Detector	: UV 220 nm
Injection volume	:20 µL
Flow rate	:1.4 mL/min

[System suitability test]

◆System performance

Resolution (1-a, 2) : 6.4 (≧5)

◆System repeatability

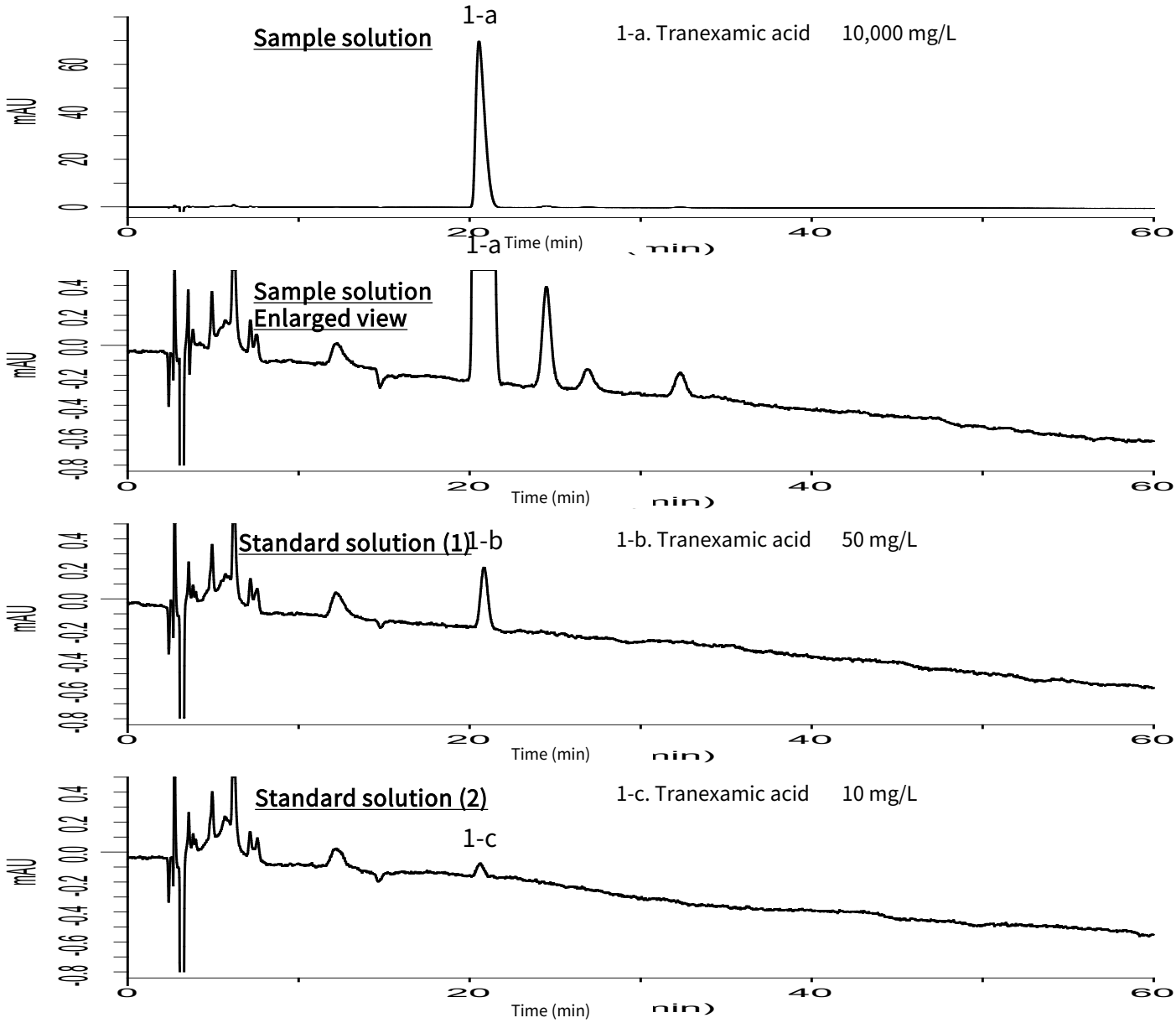
Peak area of tranexamic acid (1-b)
Relative standard deviation(%) (n=6) : 0.02 (≦0.6)

*1 phosphate buffer
Dissolve 11.0 g of anhydrous sodium dihydrogen phosphate in 500 mL ultrapure water,
Add, triethylamine 5 mL and sodium lauryl sulfate 1.4 g
Adjust to pH 2. 5 with phosphoric acid or a solution of phosphoric acid (1 in 10).
Make up to a total volume of 600 mL.

Tranexamic Acid Purity

*Adjust the flow rate so that the retention time of tranexamic acid is approx. 20 minutes.

1-a. Tranexamic acid 10,000 mg/L



1-b. Tranexamic acid 50 mg/L

1-c. Tranexamic acid 10 mg/L

HPLC conditions

Column	: InertSustain AQ-C18 (5 µm, 250 x 6.0 mm I.D.)
Eluent	: A) Phosphate buffer *1 B) CH_3OH A/B = 60/40, v/v
Temperature	: 25 ˚C
Detector	:UV 220 nm
Injection volume	:20 µL
Flow rate	:1.4 mL/min

[System suitability test]

◆System performance
Proceed as directed in the system suitability in the Assay.

◆Test for required detectability
Peak area (1-c)/peak area (1-b) x 100 = 17.4% (14 % - 26 %)

◆System repeatability
Peak area of tranexamic acid (1-b)
Relative standard deviation(%) (n=6) : 2.1 (≦7)

*1 phosphate buffer
Dissolve an 11.0 g of anhydrous sodium dihydrogen phosphate in 500 mL water,
Add 5 mL triethylamine and 1.4 g sodium lauryl sulfate
Adjust to pH 2. 5 with phosphoric acid or a solution of phosphoric acid (1 in 10).
Add water to make up to a total volume of 600 mL.

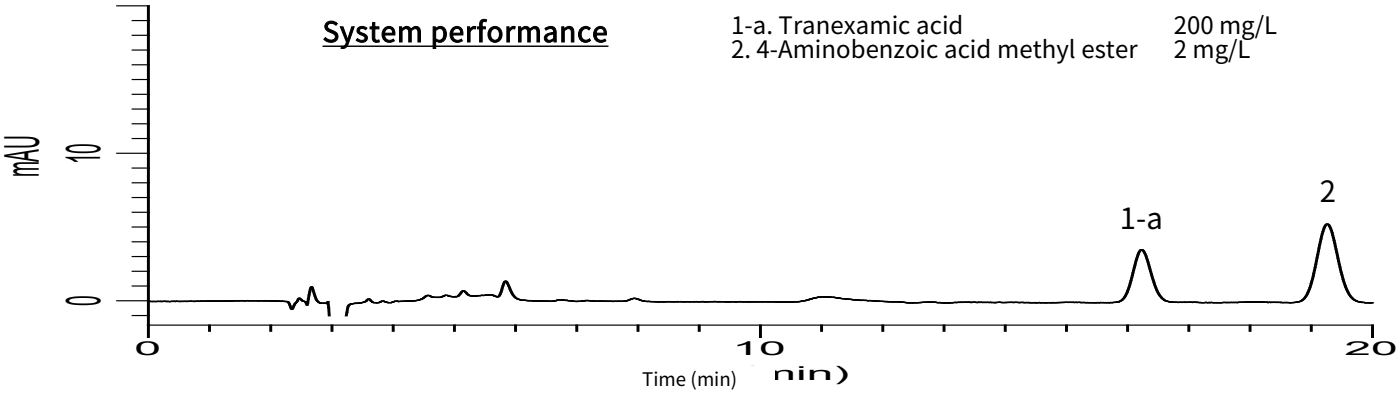
*No related substances were identified.

Tranexamic Acid Tablet Assay

*Adjust the flow rate so that the retention time of tranexamic acid is approx.16 minutes.

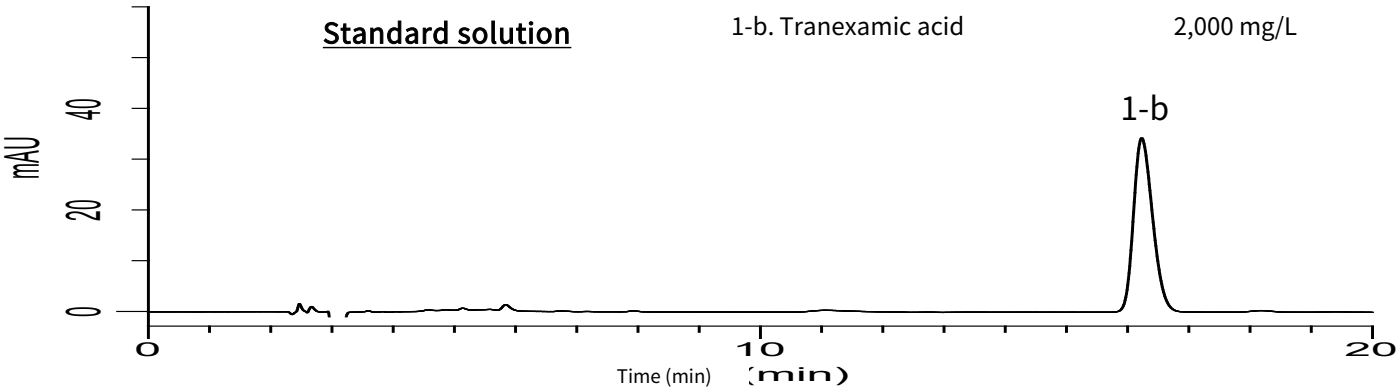
System performance

1-a. Tranexamic acid 200 mg/L
2. 4-Aminobenzoic acid methyl ester 2 mg/L



Standard solution

1-b. Tranexamic acid 2,000 mg/L



HPLC conditions (Green letters: Note the values.)

Column	: InertSustain AQ-C18 (5 µm, 250 x 6.0 mm I.D.)
Eluent	: A) Phosphate buffer *1 B) CH_3OH A/B = 60/40, v/v
Temperature	: 35 ˚C
Detector	: UV 220 nm
Injection volume	: 30 µL
Flow rate	: 1.45 mL/min

[System suitability test]

◆System performance

Resolution (1-a, 2) : 5.1 (≧3)

◆System repeatability

Peak area of tranexamic acid (1-b)
Relative standard deviation(%) (n=6) : 0.07 (≦1.0)

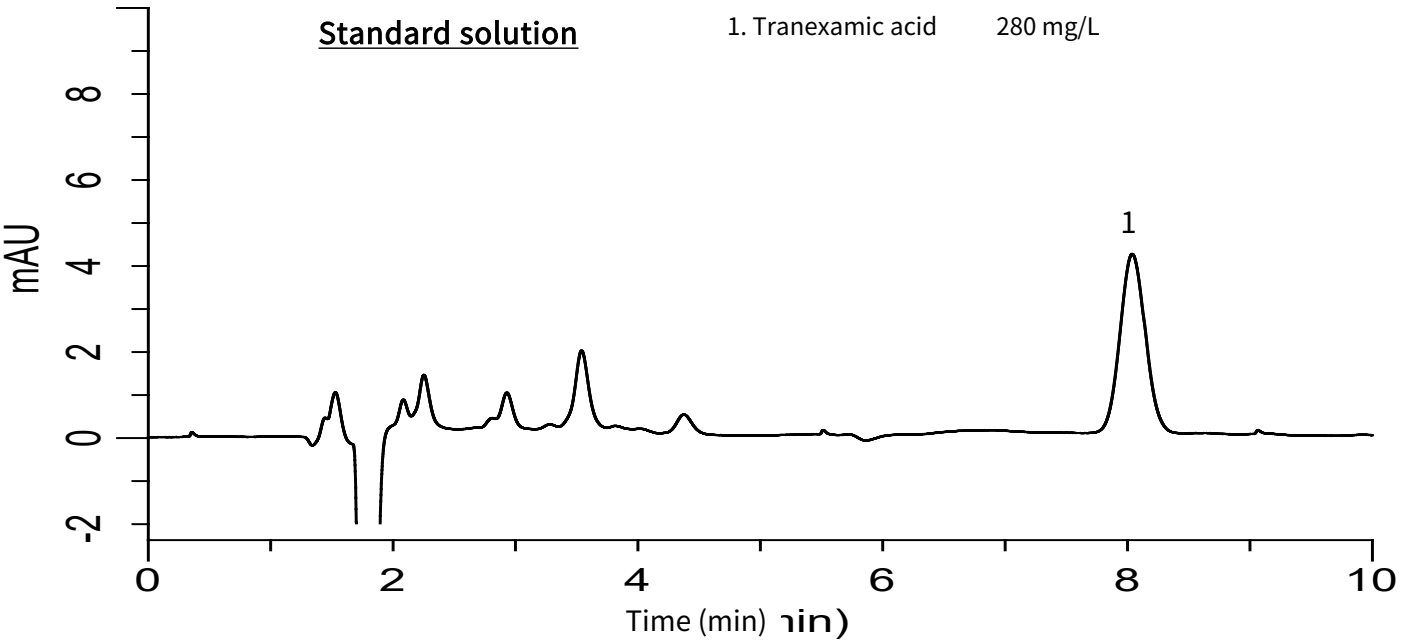
*1 phosphate buffer
Dissolve 11.0 g of anhydrous sodium dihydrogen phosphate in 500 mL ultrapure water,
Add 5 mL triethylamine and 1.4 g sodium lauryl sulfate
Adjust to pH 2. 5 with phosphoric acid or a solution of phosphoric acid (1 in 10).
Add water to make up to 600 mL.

*The sample solution has not been measured.

In the assay under "Tranexamic Acid Capsules" and "Tranexamic Acid Injection", The same analytical conditions as above are used to define the test method.

Tranexamic Acid Capsule Dissolution

*Adjust the flow rate so that the retention time of tranexamic acid is approx. 8 minutes.



HPLC conditions (Green letters: Note the values.)

Column	: Inertsil ODS-4 (5 µm, 150 x 4.6 mm I.D.)
Eluent	: A) Phosphate buffer *2 B) CH_3OH A/B = 60/40, v/v
Temperature	: 25 ˚C
Detector	:UV 220 nm
Injection volume	:10 µL
Flow rate	:0.9 mL/min

[System suitability test]

◆System performance

Number of theoretical plates : 6,899 (≧4,000)

Symmetry factor : 1.07 (≦2.0)

◆System repeatability

Peak area of tranexamic acid

Relative standard deviation(%) (n=6) : 0.25 (≦2.0)

*The sample solution has not been measured.

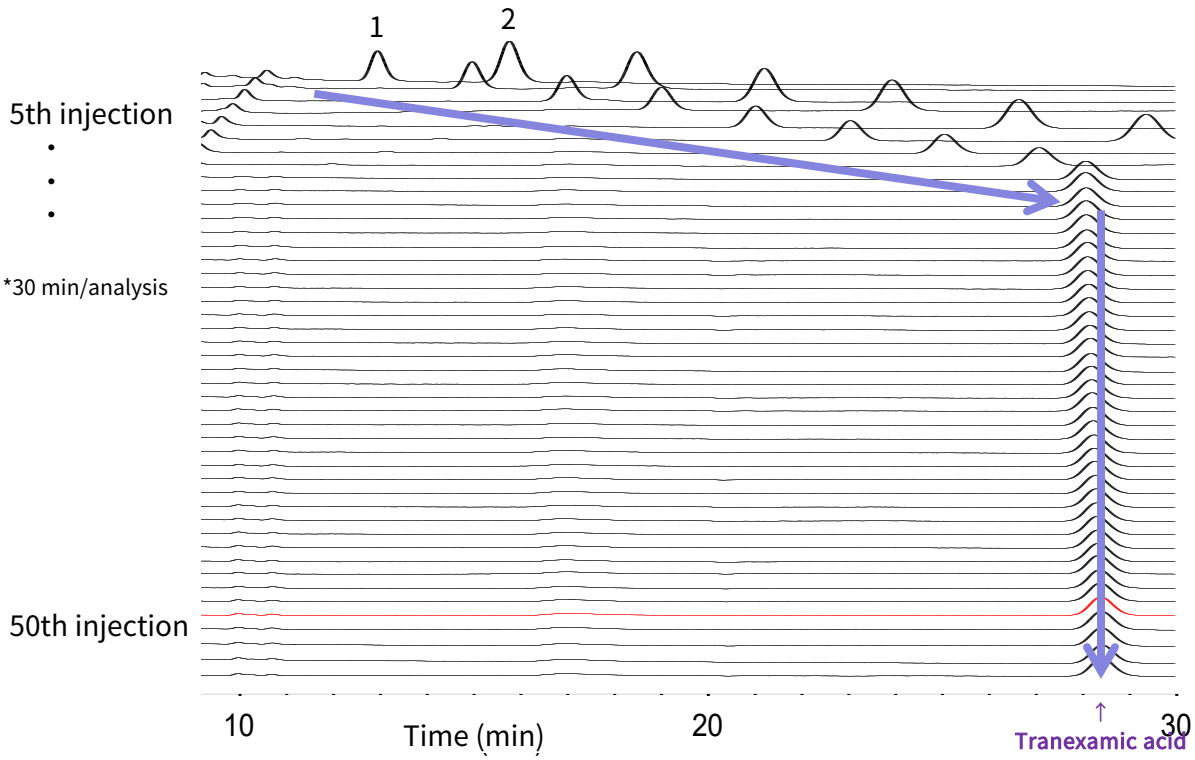
*2 phosphate buffer
Dissolve 11.0 g of anhydrous sodium dihydrogen phosphate in 500 mL ultrapure water,
Add 10 mL triethylamine and 1.4 g sodium lauryl sulfate
Adjust to pH 2. 5 with phosphoric acid or a solution of phosphoric acid (1 in 10).
Add water to make up to 600 mL.

Note on the eluent!!

1. Tranexamic acid	200 mg/L
2. 4-Aminobenzoic acid methyl ester	2 mg/L

Caution: (1) Flow a sufficient amount of eluent until the retention time is stable!

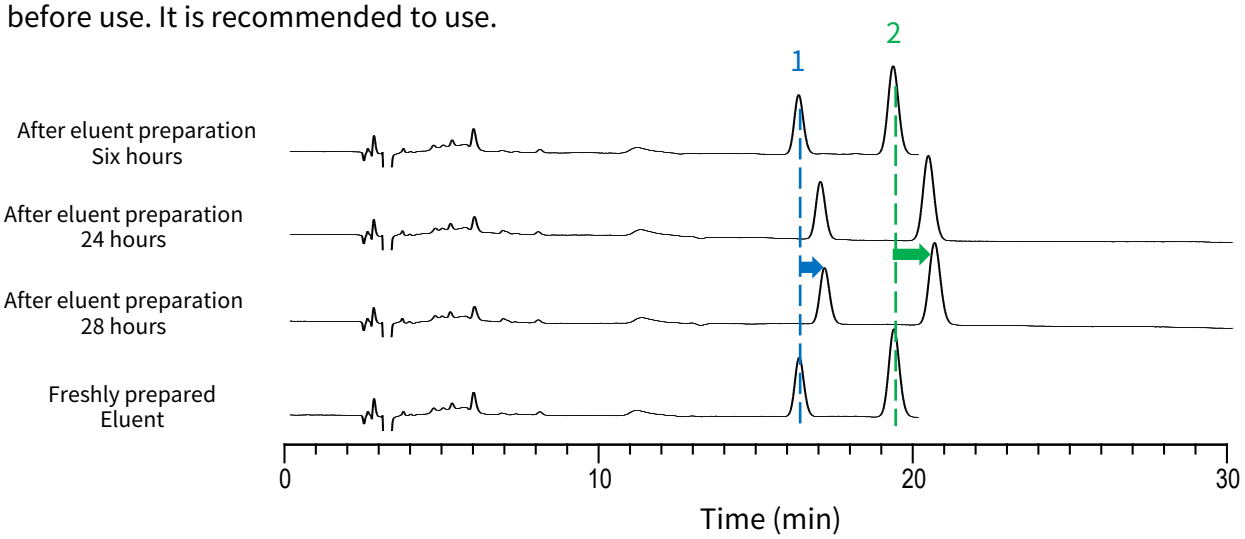
As ion-paired reagents in the eluent used for the JP17 tranexamic acid assay
Add sodium lauryl sulfate.
Because the eluent is difficult to accommodate the column, a substantial amount must be flushed until the retention time is stable.
(As a guide, continuous flow for 24 hours at a flow rate 1 mL /min.)



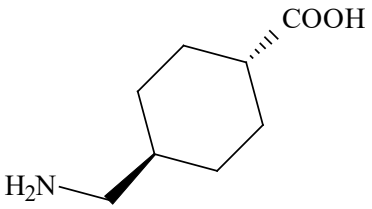
The retention time was stabilized in the 46th (approx. 23 hours after the start of eluent passage).

PRECAUTIONS (2) Use the eluent before preparation!

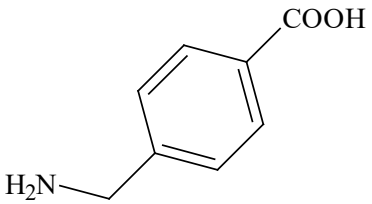
The retention time gradually increases as the eluent continues to flow over a long period of time relative to a column with a sufficient amount of displaced eluent. There is a tendency.
The freshly prepared eluate is flowed back to the original retention time, and the eluate is prepared before use. It is recommended to use.



Structural Formula



Tranexamic acid



4-(Aminomethyl) benzoic acid

Structures are created using Chemistry 4-D Draw which is provided by ChemInnovation Software, Inc.

*This data is a reference for selecting a column for customers considering pharmacopoeial analysis.
It does not guarantee the system suitability of the customer's equipment.

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