area of tocopherol nicotinate obtained from 10 μL of this
solution is equivalent to 7 to 13% of that of tocopherol
nicotinate obtained from 10 μL of the test solution for sys-
tem suitability.

System performance: Dissolve 0.05 g of Tocopherol
Nicotinate and 0.25 g of tocopherol in 100 mL of ethanol
(99.5). When the procedure is run with 10 μL of this solu-
tion under the above operating conditions, tocopherol and
tocopherol nicotinate are eluted in this order with the resolu-
tion between these peaks being not less than 8.

System repeatability: When the test is repeated 6 times
with 10 μL of the standard solution under the above operat-
ing conditions, the relative standard deviation of the peak
areas of tocopherol nicotinate is not more than 2.0%.

Assay Weigh accurately about 0.05 g each of Tocopherol
Nicotinate and Tocopherol Nicotinate Reference Standard,
dissolve each in ethanol (99.5) to make exactly 50 mL, and
use these solutions as the sample solution and the standard
solution, respectively. Perform the test with exactly 5 μL
each of the sample solution and the standard solution as
directed under the Liquid Chromatography according to the
following conditions, and determine peak areas, A_T and A_S,
of tocopherol nicotinate of these solutions.

\[
\text{Amount (mg) of } C_{15}H_{31}NO_3 = \text{amount (mg) of Tocopherol Nicotinate} \times \frac{A_T}{A_S}
\]

Operating conditions—
Detector: An ultraviolet absorption photometer
(wavelength: 264 nm).
Column: A stainless steel column 4.6 mm in inside di-
ameter and 15 cm in length, packed with octadecysilanized
silica gel for liquid chromatography (5 μm in particle di-
ameter).
Column temperature: A constant temperature of about
35°C.
Mobile phase: Methanol
Flow rate: Adjust the flow rate so that the retention time
of tocopherol nicotinate is about 10 minutes.

System suitability—
System performance: Dissolve 0.05 g of Tocopherol
Nicotinate and 0.25 g of tocopherol in 100 mL of ethanol
(99.5). When the procedure is run with 5 μL of this solu-
tion under the above operating conditions, tocopherol and
tocopherol nicotinate are eluted in this order with the resolu-
tion between these peaks being not less than 3.
System repeatability: When the test is repeated 6 times
with 5 μL of the standard solution under the above operat-
ing conditions: the relative standard deviation of the peak
areas of tocopherol nicotinate is not more than 0.8%

Containers and storage Containers—Tight containers.
Storage—Light-resistant.

**Todralazine Hydrochloride**

塩酸トララジン

C_{11}H_{12}N_2O_2.HCl.H_2O: 286.71
Ethyl 2-(phthalazin-1-yl)hydrazinecarboxylate
monohydrochloride monohydrate
[3778-76-5, anhydride]

Todralazine Hydrochloride contains not less than
98.5% of C_{11}H_{12}N_2O_2.HCl (mol. wt.: 268.70), calculated
on the anhydrous basis.

Description Todralazine Hydrochloride occurs as white
crystals or crystalline powder. It has a slight, characteristic
odor, and has a bitter taste.

It is very soluble in formic acid, freely soluble in
methanol, soluble in water, sparingly soluble in ethanol (95),
and practically insoluble in diethyl ether.

The pH of a solution of Todralazine Hydrochloride (1 in
200) is between 3.0 and 4.0.

Identification (1) To 2 mL of a solution of Todralazine
Hydrochloride (1 in 200) add 5 mL of silver nitrate-ammo-
nia TS: the solution becomes turbid, and a black precipitate
is formed.

(2) Determine the absorption spectrum of a solution of
Todralazine Hydrochloride in 0.1 mol/L hydrochloric acid
TS (3 in 100,000) as directed under the Ultraviolet-visible
Spectrophotometry, and compare the spectrum with the
Reference Spectrum: both spectra exhibit similar intensities
of absorption at the same wavelengths.

(3) Determine the infrared absorption spectrum of
Todralazine Hydrochloride as directed in the potassium
chloride disk method under the Infrared Spectrophotomet-
ry, and compare the spectrum with the Reference Spectrum:
both spectra exhibit similar intensities of absorption at the
same wave numbers.

(4) A solution of Todralazine Hydrochloride (1 in 50)
responds to the Qualitative Tests (1) for chloride.

Purity (1) Clarity and color of solution—Dissolve 0.30 g
of Todralazine Hydrochloride in 10 mL of water: the solu-
tion is clear and colorless to pale yellow.

(2) Sulfate—Proceed the test with 2.0 g of Todralazine
Hydrochloride. Prepare the control solution with 0.50 mL
of 0.005 mol/L sulfuric acid VS (not more than 0.012%).

(3) Heavy metals—Proceed with 1.0 g of Todralazine
Hydrochloride according to Method 2, and perform the
test.
Prepare the control solution with 2.0 mL of Standard Lead
Solution (not more than 20 ppm).

(4) Arsenic—Prepare the test solution with 1.0 g of
Todralazine Hydrochloride according to Method 1, and per-
farm the test using Apparatus B (not more than 2 ppm).

(5) Related substances—Dissolve 0.050 g of Todralazine
Hydrochloride in 100 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 10 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the total area of the peaks other than the peak of tofaralazine from the sample solution is not larger than the peak area of tofaralazine from the standard solution.

Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 240 nm).
Column: A stainless steel column 3.9 mm in inside diameter and 30 cm in length, packed with octadeclsilanized silica gel for liquid chromatography (10 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: Dissolve 1.10 g of sodium 1-heptane sulfonate in 1000 mL of diluted methanol (2 in 5). Adjust the pH of the solution to between 3.0 and 3.5 with acetic acid (100).
Flow rate: Adjust the flow rate so that the retention time of tofaralazine is about 8 minutes.
Time span of measurement: About twice as long as the retention time of tofaralazine after the solvent peak.

System suitability—
Test for required detection: To exactly 5 mL of the standard solution add the mobile phase to make exactly 25 mL. Confirm that the peak area of tofaralazine obtained from 10 μL of this solution is equivalent to 15 to 25% of that of tofaralazine obtained from 10 μL of the standard solution.
System performance: Dissolve 5 mg each of Tofasalazine Hydrochloride and potassium biphthalate in 100 mL of the mobile phase. When the procedure is run with 10 μL of this solution under the above operating conditions, pthalic acid and tofaralazine are eluted in order with the resolution between these peaks being not less than 8.
System repeatability: When the test is repeated 6 times with 10 μL of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of tofaralazine is not more than 2.0%.

Water 6.0 – 7.5% (0.5 g, direct titration).
Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.4 g of Tofasalazine Hydrochloride, dissolve in 5 mL of formic acid, add 70 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS = 26.870 mg of C₁₉H₁₉N₂O₄·HCl

Containers and storage Containers—Tight containers.

Tofasalazine

\[ C_{23}H_{30}N_2O_6; 382.45 \]

\((R5)\)-1-(3,4-Dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-2,3-benzodiazepine [22345-47-7]

Tofasalazine, when dried, contains not less than 98.0% of \( C_{23}H_{30}N_2O_6 \).

Description Tofasalazine occurs as a pale yellowish white, crystalline powder.

It is freely soluble in acetic acid (100), soluble in acetone, sparingly soluble in ethanol (95), slightly soluble in diethyl ether, and practically insoluble in water.

A solution of Tofasalazine in ethanol (95) (1 in 100) shows no optical rotation.

Identification (1) Determine the absorption spectrum of a solution of Tofasalazine in ethanol (95) (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Tofasalazine, previously dried, as directed in the potassium bromide disk method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

Melting point 155 – 159°C

Purity (1) Heavy metals—Proceed with 1.0 g of Tofasalazine according to Method 2, and perform the test. Prepare the control solution with 1.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Arsenic—Proceed the test solution with 1.0 g of Tofasalazine according to Method 3, and perform the test using Apparatus B (not more than 2 ppm).

(3) Related substances—Dissolve 0.05 g of Tofasalazine in 10 mL of acetone, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add acetone to make exactly 25 mL, pipet 1 mL of this solution, add acetone to make exactly 20 mL, and use this solution as the standard solution. Perform the test with these solutions as directed under the Thin-layer Chromatography. Spot 10 μL each of the sample solution and the standard solution on a plate of silica gel with fluorescent indicator for thin-layer chromatography. Develop the plate with a mixture of ethyl acetate, acetone, methanol and formic acid (24:12:2:1) to a distance of about 10 cm, and air-dry the plate. Examine under ultraviolet light (main wavelength: 254 nm): the spots