(3) Evaporate 1 mL of Compound Oxycodone Injection on a water bath. Dissolve the residue in 3 mL of sulfuric acid, add 2 drops of a solution of tannic acid in ethanol (95) (1 in 20), and allow to stand: a deep green color is produced (hydrocotarnine).

Assay Pipet 2 mL of Compound Oxycodone Injection, add exactly 10 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.4 g of oxycodone hydrochloride for assay and about 0.1 g of hydrocotarnine hydrochloride for assay previously dried at 105°C for 3 hours, and dissolve in water to make exactly 50 mL. Pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution, 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. Calculate the ratios, Q_{Ta} and Q_{Tb}, of the peak area of oxycodone hydrochloride and hydrocotarnine hydrochloride to that of the internal standard from the sample solution, and the ratios, Q_{Sa} and Q_{Sb}, of the peak area of oxycodone hydrochloride and hydrocotarnine hydrochloride to that of the internal standard from the standard solution.

Amount (mg) of oxycodone hydrochloride ($C_{18}H_{21}NO_4.HCl.3H_2O$)
= amount (mg) of oxycodone hydrochloride for assay, calculated on the anhydrous basis

$$\times \frac{Q_{Ta}}{Q_{Sa}} \times 1.1536 \times \frac{1}{25}$$

Amount (mg) of hydrocotarnine hydrochloride ($C_{12}H_{15}NO_3.HCl.H_2O$)
= amount (mg) of hydrocotarnine hydrochloride for assay

$$\times \frac{Q_{Tb}}{Q_{Sb}} \times 1.0699 \times \frac{1}{25}$$

Internal standard solution—Dissolve 0.02 g of phenacetin in 10 mL of ethanol (95), and add water to make 100 mL.
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 285 nm).
Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized polyvinyl alcohol gel polymer for liquid chromatography (5 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: To 500 mL of 0.05 mol/L disodium hydrogenphosphate TS add 0.05 mol/L sodium dihydrogenphosphate TS, and adjust the pH to 8.0. To 300 mL of this solution add 200 mL of acetonitrile, and mix.
Flow rate: Adjust the flow rate so that the retention time of oxycodone hydrochloride is about 8 minutes.
Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and use a column giving elution of the internal standard, oxycodone hydrochloride and hydrocotarnine hydrochloride in this order, and complete separation of their peaks.

Containers and storage Containers—Hermetic containers, and colored containers may be used.
Storage—Light-resistant.

Compound Oxycodone and Atropine Injection

Hycoato Injection

複方オキシコドン・アトロピン注射液

Compound Oxycodone and Atropine Injection is an aqueous solution for injection.
It contains not less than 0.74 w/v% and not more than 0.86 w/v% of oxycodone hydrochloride ($C_{18}H_{21}NO_4.HCl.3H_2O$: 405.87), not less than 0.18 w/v% and not more than 0.22 w/v% of hydrocotarnine hydrochloride ($C_{12}H_{15}NO_3.HCl.H_2O$: 275.73), and not less than 0.027 w/v% and not more than 0.033 w/v% of atropine sulfate [$(C_{17}H_{23}NO_3)_2.H_2SO_4.H_2O$: 694.83].

Method of preparation

Oxycodone Hydrochloride	8 g
Hydrocotarnine Hydrochloride	2 g
Atropine Sulfate	0.3 g
Water for Injection	a sufficient quantity
	To make 1000 mL

Prepare as directed under Injections, with the above ingredients.

Description Compound Oxycodone and Atropine Injection is a colorless or pale yellow, clear liquid.
It is affected by light.
pH: 2.5 - 4.0

Identification (1) To 1 mL of Compound Oxycodone and Atropin Injection add 1 mL of 2,4-dinitrophenylhydrazine-ethanol TS: a yellow precipitate is formed (oxycodone).
(2) Evaporate 1 mL of Compound Oxycodone and Atropin Injection on a water bath, and dissolve the residue in 2 mL of sulfuric acid: a yellow color is produced. Heat the solution: it changes to red, and then to deep orange-red (hydrocotarnine).
(3) Evaporate 1 mL of Compound Oxycodone and Atropin Injection on a water bath. Dissolve the residue in 3 mL of sulfuric acid, add 2 drops of a solution of tannic acid in ethanol (95) (1 in 20), and allow to stand: a deep green color is produced (hydrocotarnine).
(4) To 1 mL of Compound Oxycodone and Atropine Injection add 0.5 mL of 2,4-dinitrophenylhydrazine-ethanol TS, and allow to stand for 1 hour. Centrifuge, and add acetone to the supernatant liquid until no more precipitate is produced. Allow to stand for 20 minutes, and centrifuge. To the supernatant liquid add potassium hydroxide TS until the liquid is light purple. Shake the liquid with 5 mL of dichloromethane, and separate the dichloromethane layer. Take 0.5 mL of the dichloromethane layer, and evaporate to dryness on a water bath. Add 5 drops of fuming nitric acid to the residue, and evaporate to dryness on a water bath. Cool, dissolve the residue in 1 mL of *N,N*-dimethylformamide, and add 6 drops of tetraethylammonium hydroxide TS: a red-purple color is produced (atropine).

Assay (1) Oxycodone hydrochloride and hydrocotarnine hydrochloride—Pipet 2 mL of Compound Oxycodone and

Atropine Injection, add exactly 10 mL of the internal standard solution, and use this solution as the sample solution. Separately, weigh accurately about 0.4 g of oxycodone hydrochloride for assay and about 0.1 g of hydrocotarnine hydrochloride for assay previously dried at 105°C for 3 hours, and dissolve in water to make exactly 50 mL. Pipet 2 mL of this solution, add exactly 10 mL of the internal standard solution, 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. Calculate the ratios, Q_{Ta} and Q_{Sb}, of the peak area of oxycodone hydrochloride and hydrocotarnine hydrochloride to that of the internal standard from the sample solution, and the ratios, Q_{Sa} and Q_{Sb}, of the peak area of oxycodone hydrochloride and hydrocotarnine hydrochloride to that of the internal standard from the standard solution.

Amount (mg) of oxycodone hydrochloride ($C_{18}H_{21}NO_4.HCl.3H_2O$)
= amount (mg) of oxycodone hydrochloride for assay, calculated on the anhydrous basis
$\times \frac{Q_{Ta}}{Q_{Sa}} \times 1.1536 \times \frac{1}{25}$

Amount (mg) of hydrocotarnine hydrochloride ($C_{12}H_{15}NO_3.HCl.H_2O$)
= amount (mg) of hydrocotarnine hydrochloride for assay
$\times \frac{Q_{Tb}}{Q_{Sb}} \times 1.0699 \times \frac{1}{25}$

Internal standard solution—Dissolve 0.02 g of phenacetin in 10 mL of ethanol (95), and add water to make 100 mL.
Operating conditions—
Detector: An ultraviolet absorption photometer (wavelength: 285 nm).
Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized polyvinyl alcohol gel polymer for liquid chromatography (5 μm in particle diameter).
Column temperature: A constant temperature of about 25°C.
Mobile phase: To 500 mL of 0.05 mol/L disodium hydrogenphosphate TS add 0.05 mol/L sodium dihydrogenphosphate TS, and adjust the pH to 8.0. To 300 mL of this solution add 200 mL of acetonitrile, and mix.
Flow rate: Adjust the flow rate so that the retention time of oxycodone hydrochloride is about 8 minutes.
Selection of column: Proceed with 10 μL of the standard solution under the above operating conditions, and use a column giving elution of the internal standard, oxycodone hydrochloride and hydrocotarine hydrochloride in this order, and complete separation of their peaks.

(2) Atropine sulfate—Pipet 2 mL of Compound Oxycodone and Atropine Injection, and add exactly 2 mL of the internal standard solution. To this solution add 10 mL of diluted dilute hydrochloric acid (1 in 10) and 2 mL of ammonia TS, immediately add 20 mL of dichloromethane, shake vigorously, filter the dichloromethane layer through filter paper on which 5 g of anhydrous sodium sulfate is placed, and evaporate the filtrate to dryness under reduced pressure. To the residue add 0.5 mL of 1,2-dichloromethane and 0.5 mL of bis-trimethylsilylacetamide, stopper tightly, warm in a water bath at 60°C for 15 minutes, and use this solution as the sample solution. Separately, weigh accurately about 0.03 g of Atropine Sulfate Reference Standard (separately determine its loss on drying in the same manner as directed under Atropine Sulfate), and dissolve in water to make exactly 100 mL. Pipet 2 mL of this solution, and add exactly 2 mL of the internal standard solution. Proceed with this solution in the same manner as directed as for the sample solution, and use so obtained solution as the standard solution. Perform the test with 2 μL each of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of atropine to that of the internal standards.

Amount (mg) of atropine sulfate [$(C_{17}H_{23}NO_3)_2.H_2SO_4.H_2O$]
= amount (mg) of Atropine Sulfate Reference Standard, calculated on the dried basis
$\times \frac{Q_T}{Q_S} \times \frac{1}{50} \times 1.027$

Internal standard solution—A solution of homatropine hydrobromide (1 in 4000).
Operating conditions—
Detector: A hydrogen flame-ionization detector.
Column: A glass column about 3 mm in inside diameter and about 1.5 m in length, packed with 180- to 250-μm siliceous earth for gas chromatography coated with 1 to 3% of 50% phenyl-methylsilicone polymer.
Column temperature: A constant temperature of about 210°C.
Carrier gas: Nitrogen or helium.
Flow rate: Adjust the flow rate so that the retention time of atropine is about 5 minutes.
Selection of column: Proceed with 2 μL of the standard solution under the above operating conditions, and calculate the resolution. Use a column giving elution of the internal standard and atropine in this order with the resolution between these peaks being not less than 3.

Containers and storage Containers—Hermetic containers, and colored containers may be used.
Storage—Light-resistant.

Oyster Shell

Ostreae Testa

ボレイ

Oyster Shell is the shell of *Ostrea gigas* Thunberg (*Ostreidae*).

Description Irregularly curved, foliaceous or lamellated broken pieces. The unbroken oyster shell forms a bivalve 6 - 10 cm in length and 2 - 5 cm in width. The upper valve is flat and the lower one is somewhat hollow. Both the upper and lower edges of the valve are irregularly curved and bite with each other. The surface of the valve is externally light greenish gray-brown and internally milky in color. Odorless and tasteless.

Identification **(1)** Dissolve 1 g of sample pieces of Oyster