

Application News

Total Organic Carbon Analysis

No. O37

Swab / Direct Combustion Carbon Analysis of Drug Residue by TOC-VCPH

Cleaning validation for production equipment at pharmaceutical facilities is an evaluation examination that is conducted to prevent cross-contamination from previously processed products and contamination due to foreign material. It is therefore an important process for ensuring quality control and safety. HPLC (high performance liquid chromatography) systems are used to evaluate and test for the presence of drug residues in pharmaceutical production equipment. However, when sample preparation requires the use of solvent extraction or enrichment, etc., this method can become quite complicated and time-consuming. On the other hand, since measurement using a TOC (Total Organic Carbon) analyzer requires no sample preparation, the quantity of drug residues can be quickly and easily detected. The rinse method and swab method are two major sampling methods used in cleaning validation, however, the United States FDA and Japanese Ministry of Health, Labour and Welfare evaluate highly and recommend the swab method. In the swab method, a fixed area of the equipment surface is

wiped with the swab material, and the residues adhering to the material are physically collected and analyzed. This allows sampling by just wiping up adhering substances, which are often difficult to sample by the rinse method if any of the adhering substances are insoluble.

Using the "swab / direct combustion carbon analysis method" with the combination of Shimadzu's TOC analyzer with the SSM-5000A Solid Sample Combustion Unit allows direct measurement of the carbon with the SSM-5000A. This is contingent on the use of a swab that consists only of inorganic material. Thus, quick, accurate measurement can be conducted even when there are insoluble residues, which are difficult to extract with water. Furthermore, no special pretreatment procedures are required to extract residues from the swab (see steps in Fig. 1.).

This Application News introduces an example of measurement of a drug substance using the TOC-VCPH Total Organic Carbon Analyzer with the SSM-5000A Solid Sample Combustion Unit.

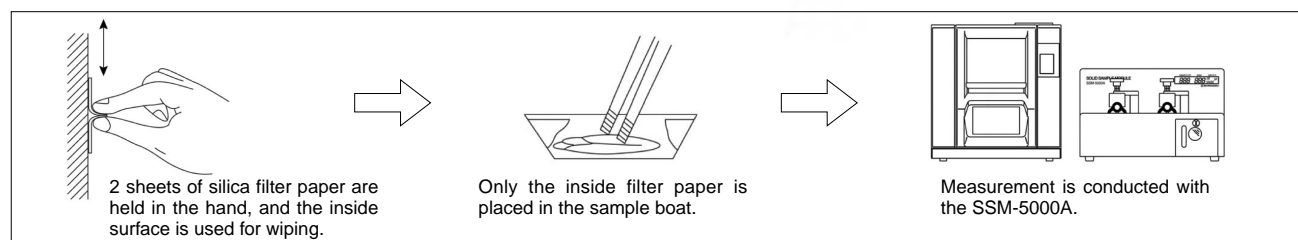


Fig. 1 Residue Evaluation Procedure Using Swab / Direct Combustion Carbon Analysis Method

■ TC Measurement of Drug Substance

Aqueous solutions of caffeine (anhydrous), acetaminophen and tranexamic acid were prepared, and the concentrations of the carbon were measured with the SSM-5000A Solid Sample Combustion Unit. These substances are drug ingredients that are normally used in typical combination cold remedies.

Each substance was dissolved in purified water to prepare a 1000 mgC/L (equivalent to 1000 mg/L carbon concentration) solution, and these solutions (100 μ L each) were transferred to sample boats and then covered with heat-treated quartz silica fiber filter paper to be impregnated with the solutions. The organic carbon concentrations were then measured using the SSM-5000A. The results are shown in Table 1.

The instrument was calibrated by generating a calibration curve using 30 μ L of 1 % C glucose solution.

Analytical Conditions

Instrument	: Shimadzu TOC-VCPH Total Organic Carbon Analyzer + SSM-5000A Solid Sample Combustion Unit
Measurement item	: TC
Calibration curve	: Generated using 30 μ L of 1 % C glucose solution
Samples	: (1) 1000 mgC/L caffeine solution prepared by dissolving 202.1 mg caffeine (anhydrous) in 100 mL purified water (2) 1000 mgC/L acetaminophen solution prepared by dissolving 157.2 mg acetaminophen in 100 mL purified water (3) 1000 mgC/L tranexamic acid solution prepared by dissolving 163.6 mg tranexamic acid in 100 mL purified water

Table 1 Drug Substance Measurement Data Acquired Using SSM-5000A

Sample Name	TC Measurement Value [mgC/L]
(1) 1000 mgC/L caffeine solution	949.6
(2) 1000 mgC/L acetaminophen solution	957.5
(3) 1000 mgC/L tranexamic acid solution	964.6

■ Recovery of Drug Substances by Swab / Direct Combustion Carbon Analysis Method Using SSM-5000A

Next, 100 μL each of these solutions was spread on a glass plate, and wiped dry with sheets of quartz silica fiber filter paper. These were placed in sample boats and their carbon concentrations were measured using the SSM-5000A Solid Sample Combustion Unit to test the rate of recovery. For blank measurement using the swabbing operation, distilled water was similarly spread on a glass plate and wiped dry for measurement and used as the blank. Values for the blank were 0.

The results are shown in Fig. 2 and Table 3. All the solutions showed recovery greater than 95%, confirming that accurate measurement can be conducted using the swab / direct combustion carbon analysis method.

Analytical Conditions

Instrument	: Shimadzu TOC-V _{CPH} Total Organic Carbon Analyzer + SSM-5000A Solid Sample Combustion Unit
Measurement item	: TC
Swab material	: ADVANTEC QR-100 quartz silica fiber filter paper (size 45 mm) heat-treated at 600 °C for 15 min
Measurement method	: 100 μL sample solution was spread out on a 5 cm \times 5 cm glass plate, then wiped dry with swab material moistened with 400 μL distilled water. The entire piece of swab material was then subjected to combustion measurement.

Table 2 Recovery of Drug Substances Using Swab / Direct Combustion Carbon Analysis Method

Sample Name	TC Measurement Value [μgC]	Theoretical Value [μgC]	Recovery (TC Measurement Value / Theoretical Value)
Blank (distilled water)	0	0	—
(1) 1000 mgC/L caffeine solution	92.2	95.0	97.1%
(2) 1000 mgC/L acetaminophen solution	96.0	95.8	100.2%
(3) 1000 mgC/L tranexamic acid solution	94.6	96.5	98.0%

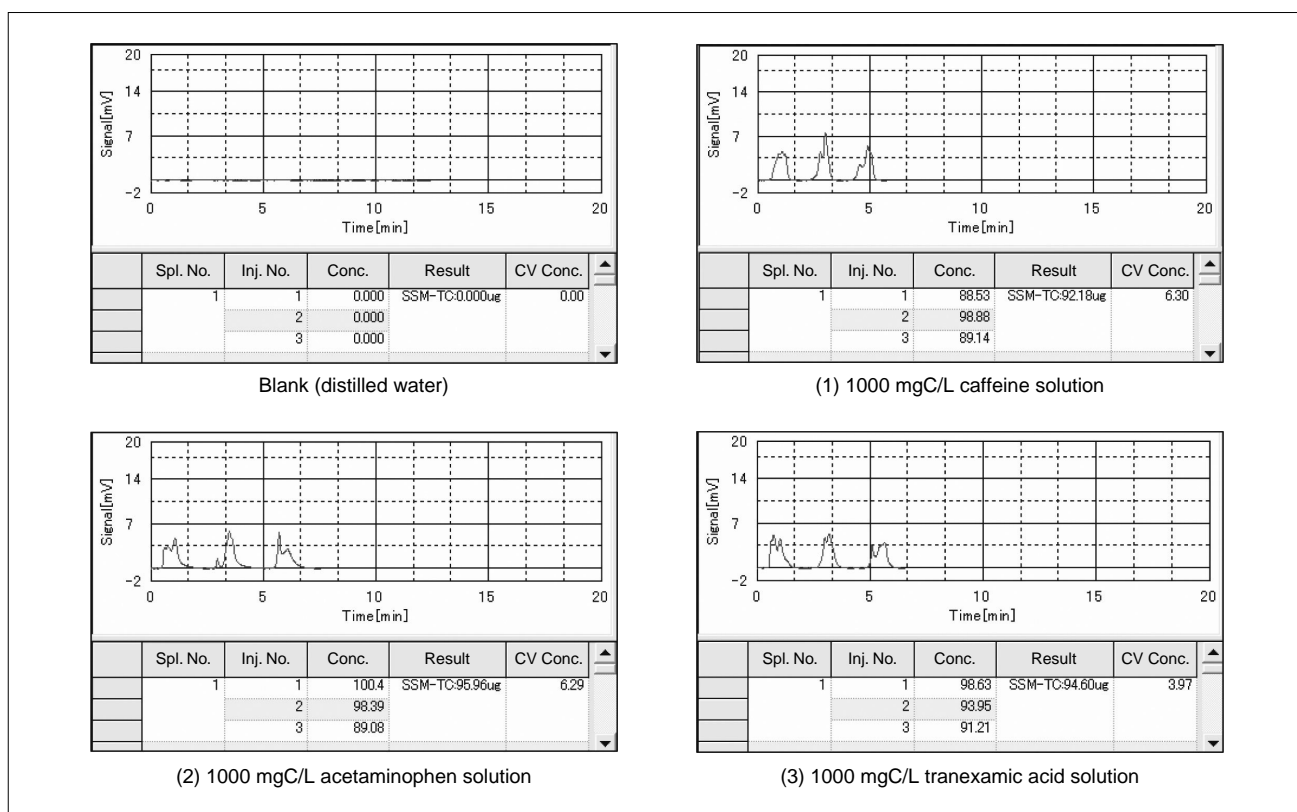


Fig. 2 Recovery of Drug Substances by Swab / Direct Combustion Carbon Analysis Method

NOTES:

*This Application News has been produced and edited using information that was available when the data was acquired for each article. This Application News is subject to revision without prior notice.



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