

High Sensitivity Total Organic Carbon Analysis

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Introduction

In the last decade, there has been an increase in demand for total organic carbon (TOC) analysers that can analyse TOC in part per billion (ppb) level from industries such as pharmaceutical¹⁰, biomedical³, electronic^{2, 5}, filter manufacturers and power plant operators. The process water used in these industries must have low TOC level to produce high quality products.

The Shimadzu TOC analyser, the TOC-5000/5000A is widely used in the pharmaceutical industry. According to United States Pharmacopoeia 25¹⁰ that is widely used in the pharmaceutical industry, the TOC analyser is required to have a manufacturer's specified limit of detection of 50 ppb and the TOC level in the water samples should not exceed 500 ppb. A number of articles have been published which demonstrate that the 680°C platinum catalytic combustion/non-dispersive infrared (NDIR) method used in TOC-5000/5000A can meet these high sensitivity requirements in the pharmaceutical industry^{1, 4, 6, 7, 11}.

It is easier to carry out high sensitivity TOC analysis using the newer models, the TOC-VCSH/CPH*. The TOC-VCSH/CPH is similar to the TOC-5000/5000A but it has additional features and functions. Functions such as auto-addition of acid and sparging within syringe for non-purgeable organic carbon (NPOC) analysis, mixing and dilution can be carried out, as the TOC-VCSH/CPH is equipped with a multi-functional 8-port valve and 5 ml syringe.

A high sensitivity TOC analysis using the TOC-VCSH is shown below. Another model, the TOC-VWP was also used as a comparison. Unlike the TOC-VCSH that uses the catalytic combustion oxidation method, the TOC-VWP uses a combination of persulfate reagents, UV and heat to oxidise carbon compounds to carbon dioxide (CO₂), which is then measured with a NDIR detector.

Methods & Results

In the first part of the experiment, the TOC-VCSH was used. Commercially available cylinders filled with purified air or nitrogen was used. According to the gas manufacturer, the hydrocarbon content was less than 5 ppm. Ultra pure water used in this experiment was produced by deionised, reverse osmosis, electrodeionisation, UV and finally filtered by a 0.22 µm filter to produce resistivity of 18 MΩ using the Milli-Q system from Millipore, USA.

The total carbon (TC) standard solution was prepared using potassium hydrogen phthalate (COOH.C₆H₄.COOK) from Nacalai Tesque, Japan. Concentrated hydrochloric acid, 37% (HCl) and phosphoric acid, 85% (H₃PO₄) was purchased from J T Baker, USA whereas sodium persulfate (Na₂S₂O₈) was obtained from Aldrich Chemicals, USA.

The NPOC method was used to minimise the effect of CO₂ from the atmosphere. Each standard solution/sample was automatically drawn into the syringe followed by auto-addition of 2M HCl to lower the pH to 2. Then, sparging was carried out inside the syringe to remove the inorganic carbon (IC). The sparged solution was then injected automatically into the 680°C quartz combustion tube filled with platinum catalyst. Finally, the CO₂ formed was carried by the carrier air into the NDIR detector to be quantified. The air used for sparging was the same as the carrier gas.

In the TOC-5000/5000A, external sparging is used where the sparging tube is placed inside the sample container. In this case, IC removal efficiency depends on the sample volume, size and shape of the sample container. The removal of IC in TOC-VCSH is more efficient as the sample is not exposed to atmospheric CO₂ and this in turn minimises any changes in IC content in sample. Furthermore, only a small volume is sparged and the syringe also has lower volume. Auto-addition of HCl to sample also makes it easier for user.

As high sensitivity analysis was involved, precautions have to be taken to minimise carbon contamination from the environment as well as reduce the CO₂ effect from the atmosphere. Some of these precautions are⁹:

- using tightly sealed clean glass containers.
- preparing the TC stock standard solutions just before measurement.
- filling TOC-VCSH diluent bottle and the rinse bottle for ASI-V auto sampler with fresh ultra pure water.
- rinsing the glassware with ultra pure water prior to use.
- injecting ultra pure water as unknown sample several times before generating the calibration curve and just before analysing the samples to 'wash' the platinum catalyst and flow line in order to stabilise the instrument and reduce the noise level.
- using a TOC-VCSH that is used to analyse samples with TOC in low ppb level only. If the TOC analyser is also used to analyse samples with TOC in part per million (ppm) levels, this would 'contaminate' the platinum catalyst and flow line, resulting in higher noise level, and subsequently increasing the detection limit.
- analysing the samples immediately after collection.

Notes

*: TOC-VCSH is a standalone model
TOC-VCPH is a PC controlled model

The features in the TOC-VCSH that are useful in high sensitivity analysis are:

- it can prepare the various standard solutions from a stock solution using the built-in dilution function. Here, the stock standard solution and dilution water are drawn into the syringe and a brief sparging carries out mixing. This can reduce human error compared to manual preparation. Although the TOC-VCSH can dilute up to 50 times, a dilution factor of not more than 20 times was used to minimise any instrument error.
- 'multiple injection' function enables the instrument to prepare a single aliquot that is sufficient for all repeat measurements. With this, analysis time is reduced – this can also reduce the atmospheric CO₂ effect.

The TOC-VCSH instrument conditions are shown in Table 1. Both manual and ASI-V auto sampler methods were used.

Table 1: Instrument condition settings in TOC-VCSH

Manual and ASI-V auto sampler	Catalyst	High sensitivity
	No of syringe wash	2 times
	Sparging	5 minutes
	Amount of 2M HCl	1 %
	Injection volume	2000 µl
	No of repeats	4
	Maximum no of repeats	6
	Multiple injection	On
	Calibration curve type	Linear regression
Manual	Port no	1
ASI-V auto sampler	No of needle wash	0
	Flow line wash	2
	Port no	2

The calibration graph results obtained using manual method is shown in Table 2.

Table 2: Calibration graph results using manual method

Conc ^a	DF ^b	Area ^c	%CV ^d	SD ^e
0 ppb	H ₂ O is used	6.69	1.95	0.13
25 ppb	20	11.50	1.13	0.13
50 ppb	10	15.57	2.57	0.40
100 ppb	5	24.66	1.93	0.47
Area = 0.1785 Conc + 6.7966 (Equation 1)				
R ² = 0.9995				

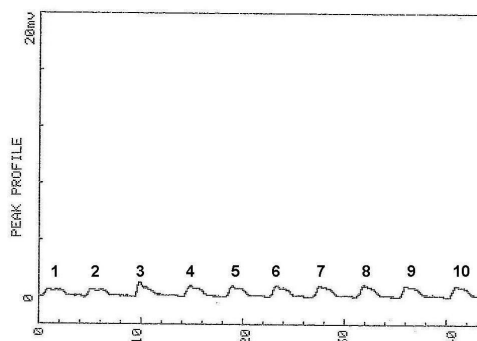
Notes

- concentration
- dilution factor when a 500 ppb TC stock solution is used
- signal produced by the TOC-V series is reported in terms of area
- percentage coefficient variation
- standard deviation

A good reproducibility was obtained as the %CV of all standard solutions was within 3%. More importantly, the regression of the calibration graph was more than 0.9990.

Next, to determine limit of detection (LOD), fresh ultra pure water was injected 10 times and the SD was recorded. LOD is defined as TOC concentration that gives a signal equivalent to 3 times the SD of noise. The peak profiles obtained are shown in Figure 1.

Figure 1: Peak profiles of 10 injections used to determine LOD



To calculate LOD, the calibration curve has to be shifted parallel to zero intercept (origin) to offset the carbon content in ultra pure water. An example of this calculation based on Equation (1) in Table 2 is shown.

Table 3: Results for 10 injections used to determine LOD

No	1	2	3	4	5
Area	4.833	5.237	7.046	6.191	6.120
No	6	7	8	9	10
Area	6.248	6.614	6.604	7.050	6.293
Mean	6.224				
SD	0.71				
%CV	11.5%				

- SD of 10 repetitions of ultra pure water = 0.71
- LOD is TOC concentration that produces signal equals to 3 x SD.
- Hence, 3 x SD = 3 x 0.71 = 2.13
- When Equation (1) is shifted to origin, it becomes Area = 0.1785 Conc
- Hence, 2.13 = 0.1785 Conc
- Conc, which is LOD = 2.13/0.1785 = 11.9 ppb

Based on the TOC-V series catalogue⁸, the TOC-VCSH has a LOD of 4 ppb. This can be achieved if new instruments are used and further precautions are taken such as placing the TOC analyser in clean environment and using purified air with hydrocarbon content less than 1 ppm. Under more common circumstances, a higher LOD is usually obtained. As shown in this experiment, a LOD of less than 50 ppb is still possible. The LOD can also be further improved by using the built-in blank check function that measures the noise from instrument and air only. In this

experiment, the noise is contributed by instrument, air and ultra pure water.

Good reproducibility was also obtained when the ASI-V auto sampler was used (Table 4).

Table 4:
Calibration graph results using ASI-V auto sampler

Conc	DF	Area	%CV	SD
25 ppb	20	8.85	2.81	0.25
50 ppb	10	14.17	0.95	0.13
100 ppb	5	24.53	1.75	0.43
Area = 0.2088 Conc + 3.667				
R ² = 0.9999				

To check the accuracy of the dilution function in the TOC-VCSH, a recovery test was carried out using a 50 ppb TC standard that was prepared manually. The concentration obtained by measurement was 49.60 ppb, a good recovery of 99.2%.

To obtain lower LOD, another Shimadzu TOC analyser, the TOC-VWP can be used. It has a LOD of 0.5 ppb⁸ compared to TOC-VCSH because the persulfate reagents used were purged first to eliminate the IC which is contributed by CO₂ in atmosphere - this helps to reduce the noise level. A larger injection volume can also be introduced into the system to give a higher signal for samples with TOC in the low ppb level. With this, more reproducible results can be obtained.

As an example, an analysis was carried out using manual method with the TOC-VWP. The precautions that were taken during analysis with the TOC-VCSH were also used here. However, unlike the TOC-VCSH, the various standard solutions were prepared manually as the TOC-VWP does not have the dilution function.

For NPOC analysis, each standard solution/sample was first automatically drawn into a glass reactor in the TOC-VWP, followed by auto-addition of 25% H₃PO₄ to lower the pH to 2. Then, sparging was carried out inside the glass reactor to remove the IC. The pre-treated standard solutions/sample and reagents are then transferred to the TC reactor for oxidation by persulfate, UV and heat. The CO₂ formed is then carried by nitrogen carrier gas into the NDIR detector.

The instrument conditions are shown in Table 5 and the results obtained are shown in Table 6.

Table 5:
Instrument condition settings in TOC-VWP

No of syringe wash	2 times
Sparging	5 minutes
Amount of wet chemical oxidant (10.5% Na ₂ S ₂ O ₈ and 3.8% H ₃ PO ₄)	1.5 ml
Amount of 25% phosphoric acid	3 %
Injection volume	20400 µl
No of repeats	4
Maximum no of repeats	6
Calibration curve type	Linear regression

Table 6:
Calibration graph results using the TOC-VWP

Conc	Area	%CV	SD
0 ppb	16.17	2.45	0.40
25 ppb	23.49	1.99	0.47
50 ppb	28.57	1.58	0.45
100 ppb	42.03	1.21	0.51
If 5 ppb standard is included	Area = 1.2753 Conc + 16.406 R ² = 0.9974		
If 5 ppb standard is not included	Area = 1.2930 Conc + 15.991 R ² = 0.9995		

From Table 6, a good reproducibility was obtained as the %CV of all standard solutions was within 3%. However, it might be more difficult to obtain calibration graph with regression of more than 0.9990 using TOC-VWP if standard solutions with very low TOC concentration were included. For example, if a 5 ppb standard solution was included in the calibration graph, the regression was less than 0.9990. This can be due to:

- as the TC concentration is low, the CO₂ effect from the atmosphere is more significant.
- unlike the TOC-VCSH, the TOC-VWP does not have dilution function to prepare standard solutions from a stock standard. Hence, each standard solution has to be prepared manually, contributing to human error.
- the TOC-VWP does not have the multiple injection function due to the large injection volume involved and the syringe could only draw the solution separately for each repeat measurement. As this increases the analysis time interval between the first and last repeat measurement, the CO₂ effect from the atmosphere is more significant.

According to ASTM D5127², the TOC requirement in Type E-1 water that is used in the production of electronic devices having dimensions larger than 5 µm, is maximum 25 ppb. This is within the measuring range of TOC-VWP. The TOC-VWP can also be used to measure TOC in biomedical water. According to ASTM D5196³, the maximum TOC concentration is 20 ppb, a level that can also be measured by TOC-VWP.

Conclusions

In this experiment, the TOC-VCSH (or the software controlled model, the TOC-VCPH) was found to have a detection limit of less than 50 ppb TOC. This fulfils the detection limit required by USP 25 in the pharmaceutical industry¹⁰. It is easier to obtain low detection limit compared to TOC-5000/5000A due to additional features in TOC-VCSH. To obtain even better sensitivity as required in the electronic² and biomedical³ fields, the TOC-VWP (or the software controlled model, the TOC-VWS) can be used.

References

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