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APPLICATION NOTE:	AN2211
TECHNOLOGY:	TOC
INDUSTRY:	Pharma

TOC Analysis for Pharmaceutical Water

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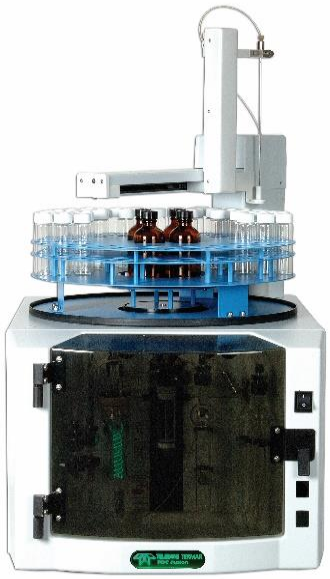
Introduction



Purified water used in the manufacturing of pharmaceutical products is constantly monitored to ensure minimal levels of contaminants. Total organic carbon (TOC) analysis is a simple and efficient way to verify that all pharmaceutical waters are within regulation. The United States Pharmacopeia (USP) states the requirement for reagent water used for bulk water procedures to be ≤0.10 mg/L TOC and ≤0.50 mg/L TOC for sterile water procedures. Limit of detection (LOD) requirements are also set by the USP for TOC instrumentation at ≤0.05 mg/L for bulk water and ≤0.10 mg/L for sterile water. The Fusion UV-persulfate TOC analyzer easily meets these requirements for monitoring water used for pharmaceutical processes.

Instrument Method

To maximize the Fusion's sensitivity at low level concentrations, the default "TOC Pharmaceutical Water" method was used as a starting point. This method was slightly modified to establish a low background. This also allowed for the signal-to-noise ratio to be optimized. Low background was accomplished by reducing the amount of phosphoric acid and sodium persulfate reagent added to each sample. Considering purified water has essentially no inorganic carbon fraction, the acid volume was reduced to 0.1 mL. Also, since low level TOC concentrations can be effectively oxidized solely by the UV lamp, the reagent volume was reduced to 0.4 mL per sample replicate. Additionally, the pre-sparge time was set to zero. One final adjustment was to turn on the low level NDIR filter which provides more baseline conditioning to achieve more system stability for low level TOC analysis.

Calibration

A five point calibration was performed using the Fusion's auto-calibration feature. A 200 µg/L standard made from potassium hydrogen phthalate (KHP) was used to build a calibration range of 10 - 200 µg/L. Calibration results are shown below in Figure 1.

Figure 1 Calibration Curve Data.

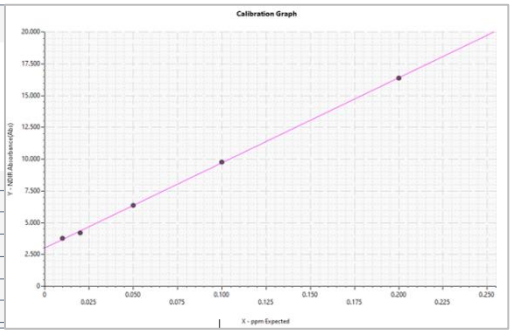
	Pos	BAT	Concentration (ppm)	STD Conc	Dil	Sample ID	Result (Abs)	Std. Dev. (Abs)	RSD
◈	A	TOC	0.0100	0.2 ppmC	1:20	[TOC] TOC Low Level [0.010 ppm]	3.7777	0.1355	3.59%
◈	A	TOC	0.0200	0.2 ppmC	1:10	[TOC] TOC Low Level [0.020 ppm]	4.2083	0.0623	1.48%
◈	A	TOC	0.0500	0.2 ppmC	1:4	[TOC] TOC Low Level [0.050 ppm]	6.3717	0.0379	0.59%
◈	A	TOC	0.1000	0.2 ppmC	1:2	[TOC] TOC Low Level [0.100 ppm]	9.7700	0.0940	0.96%
◈	A	TOC	0.2000	0.2 ppmC	1:1	[TOC] TOC Low Level [0.200 ppm]	16.3777	0.1411	0.86%

Name: TOC Pharmaceutical Water (TOC)

Version:	v20	Calibration curve formula:	y = 66.943x + 3.013
Version Creation:	2022/10/19 10:43	r^2 value:	r^2 = 0.99968
Comment:			
Operator:	SP(Appslab)		
Basic Analysis Type:	TOC		

Basic Analysis Type: TOC

Sample ID	Y Raw Value	X Expected
0.010 ppm	3.7777	0.0100
0.020 ppm	4.2083	0.0200
0.050 ppm	6.3717	0.0500
0.100 ppm	9.7700	0.1000
0.200 ppm	16.3777	0.2000



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Analysis

To demonstrate the Fusion's accuracy and precision at low levels, a series of check standards at concentrations of 0.05 mg/L and 0.10 mg/L were analyzed after calibration.

Figure 2 Check Standard Results.

Sample ID	Min / Max (% dev)	Result	Std. Dev.	RSD
[TOC] TOC Low Level [0.050 ppm]	0.0425 / 0.0575 (85% / 115%)	0.0468 ppm (PASS)	0.0026 ppm	5.56%
[TOC] TOC Low Level [0.050 ppm]	0.0425 / 0.0575 (85% / 115%)	0.0477 ppm (PASS)	0.0014 ppm	2.90%
[TOC] TOC Low Level [0.050 ppm]	0.0425 / 0.0575 (85% / 115%)	0.0462 ppm (PASS)	0.0012 ppm	2.51%
[TOC] TOC Low Level [0.100 ppm]	0.0850 / 0.1150 (85% / 115%)	0.1011 ppm (PASS)	0.0016 ppm	1.54%
[TOC] TOC Low Level [0.100 ppm]	0.0850 / 0.1150 (85% / 115%)	0.1002 ppm (PASS)	0.0005 ppm	0.48%
[TOC] TOC Low Level [0.100 ppm]	0.0850 / 0.1150 (85% / 115%)	0.0986 ppm (PASS)	0.0021 ppm	2.11%

Additionally, a purified water sample was analyzed. This result was used to calculate the LOD of the Fusion. The LOD was calculated as 3 times the standard deviation of the result, yielding LOD = 3 x 0.0004 mg/L = 0.0012 mg/L. This LOD is well below the lowest limit set by the USP of ≤0.05 mg/L for bulk water.

Figure 3 Purified Water Sample Result.

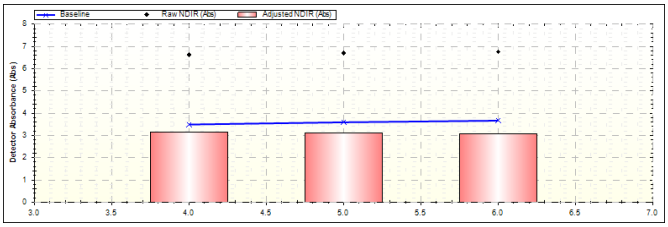
Sample Type: Sample — From Schedule Version 7

	Pos	Analysis Type	Sample ID	Result (ppmC)	Std. Dev. (ppmC)	RSD	Start Time
+	3	TOC	DI Water	0.0349 ppm	0.0004 ppm	1.0600%	2022/10/18 23:35

Rep #	Base Analysis Type	ppm	µg	Adjusted (Abs)	NDIR (Abs)	Baseline (Abs)	Pressure (psig)	Run Time
1	TOC	0.0353	0.3177	3.14	6.63	3.49	51.18	06:05
2	TOC	0.0348	0.3130	3.10	6.70	3.59	50.03	06:04
3	TOC	0.0346	0.3112	3.09	6.76	3.67	50.06	06:08

Dilution: 1:1 — Blank Contribution: (TC) 0.7740 (IC) (v43) — Method: TOC Low Level (v3) — Calibration: TOC Pharmaceutical Water (v20)

Figure 4 Graphical Results of Analysis Replicates of Purified Water Sample.



Conclusion

The data presented in this application note verifies that the Fusion UV-persulfate TOC analyzer is an excellent choice for monitoring all water types used for pharmaceutical production. The Fusion exhibits low level calibration ability in parts per billion ranges with outstanding linearity. Accurate check standard results, with precise replicate measurements, also confirm the Fusion to be the ultimate choice of reliable instrumentation for low level analysis.

References

1. United States Pharmacopeia <643> Total Organic Carbon [Revised: 01-May-2021]

See how the Teledyne Tekmar Fusion UV-persulfate analyzer can help you comply with pharmaceutical and/or environmental requirements. Contact a sales representative at 1.800.874.2004 or visit http://www.teledynetekmar.com/contact/sales-contacts. See genuine customer reviews of the Fusion at http://www.selectscience.net.