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Water & Process Technologies
Analytical Instruments

Application Note

System Suitability Testing for the Pharmaceutical Industry: TOC Analysis of Benzoquinone and Sucrose

The USP Chapter <643> requires the analysis of sucrose and benzoquinone to demonstrate system suitability for TOC analysis. The Sievers Model 800 TOC Analyzer exceeds all USP system suitability requirements for TOC analysis.

Materials

United States Pharmacopeial Convention Inc. (USP) includes requirements to analyze water for Total Organic Carbon content (TOC).[1] There are several issues that must be considered when selecting a TOC analyzer for compliance with this regulation. The most basic concern is whether the TOC analyzer will effectively measure TOC in accordance with the USP requirements.

One requirement of the regulation is to ensure that difficult-to-oxidize organic compounds are being oxidized to the same degree as easily oxidized substances and to ensure that both are accurately quantified using the TOC analyzer. The USP has selected benzoquinone as the System Suitability Compound and sucrose as a standard, or easily-oxidized substance.[2] When TOC analysis is successful for sucrose and benzoquinone, this demonstrates that the TOC analysis will be effective in monitoring a broad range of organic compounds.

This technical note describes results for the analysis of benzoquinone and sucrose using the Sievers* 800 TOC Analyzer. The data clearly demonstrates that the Sievers 800 can accurately analyze solutions of the USP System Suitability Compound benzoquinone as effectively as a Standard Solution of sucrose. This is measured by comparing the TOC recovery for the benzoquinone solution to the sucrose solution. USP states that an acceptable ratio, in terms of percentage, is 85% to 115%. The system suitability compound, benzoquinone, is assumed to be somewhat refractory and thus challenge the oxidation methods used in commercial TOC analyzers.

For this study we calibrated a Sievers 800 TOC Analyzer with potassium hydrogen phthalate (KHP), a well established calibration reference material. The calibration was accomplished using the standard protocol described within the Operating Manual for the Sievers 800. This calibration will remain stable for approximately one year.

Quantitation accuracy was confirmed using the USP recommended Standard Solution. Sucrose solutions were prepared at 500 ppb C and analyzed on three non-consecutive days prior to further analyses. **Figure 1** shows the average response for the sucrose for all three days. For these analyses, the sucrose response was 100.0%, indicating that the instrument was accurately calibrated.

After the sucrose analyses, three solutions of benzo-

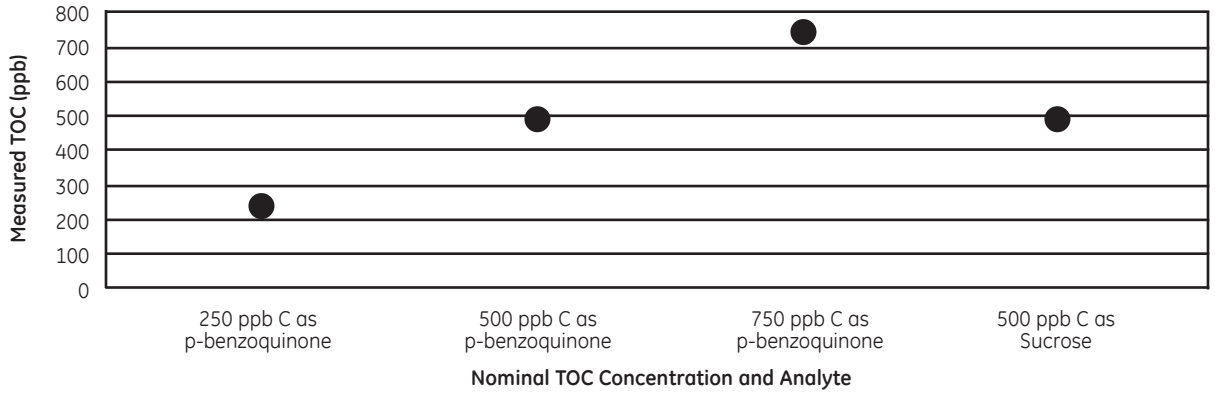

Figure 1. Analysis of p-Benzoquinone and Sucrose
Average of 5 analyses

imagination at work

Table 1. TOC Data from the Analyses of p-Benzoquinone and Sucrose Using the Sievers Model 800 TOC Analyzer

Sequence	p-benzoquinone 250 ppb	p-benzoquinone 500 ppb	p-benzoquinone 750 ppb	Sucrose 500 ppb
1	253	505	755	500
1	254	504	755	500
1	254	505	755	500
1	254	504	755	501
1	254	502	754	501
Average ± 3s	253.8 ± 1.3 ppb	504 ± 3.7 ppb	754.8 ± 1.3 ppb	500.4 ± 1.6 ppb
2	254	509	763	499
2	255	510	764	499
2	254	507	764	497
2	254	508	764	498
2	255	509	764	499
Average ± 3s	254.4 ± 1.6 ppb	508.6 ± 3.4 ppb	763.8 ± 1.3 ppb	498.4 ± 2.7 ppb
3	244	492	736	505
3	245	491	737	504
3	248	491	737	505
3	246	491	736	506
3	244	491	737	505
Average ± 3s	245.4 ± 5.0 ppb	491.2 ± 1.3 ppb	736.6 ± 1.6 ppb	505.2 ± 2.5 ppb

quinone at three different concentrations were analyzed each day. (The USP will require that a 500 ppb C solution as benzoquinone be analyzed). Results of these analyses are also presented in **Figure 1.** The data from the three concentrations demonstrate the linear response of the instrument to benzoquinone over the applicable range.

Accuracy and precision for the benzoquinone analyses were excellent. The average recovery of benzoquinone was 101%. Overall results for the nine independently prepared solutions over three days gave benzoquinone recoveries of 99–102%. Analyzing five replicates of the same 500 ppb C as benzoquinone solution gave a standard deviation range of 0.43–1.23 ppb **(see Table 1).**

These data demonstrate the effectiveness of the oxidation reactor used in the Sievers Model 800. Recovery of benzoquinone was obtained using the least aggressive oxidizing conditions available to the Model 800. Oxidation was complete using the UV lamp only; no persulfate oxidizer was required to obtain complete recovery of the sucrose or the benzoquinone. This is consistent with Ionics Instruments' recommendation that the instrument does not require the persulfate oxidizer with TOC concentrations less than 1 ppm.

The Sievers 800 TOC Analyzer demonstrates exceptional performance in TOC analysis for the USP regulations. The recovery of the sucrose and benzoquinone exceeds all of the USP requirements. With properly prepared reference standards, the response efficiency (the ratio of recovery of benzoquinone to the recovery of sucrose at 500 C) was 100%. Both benzoquinone and sucrose are accurately quantified, with excellent reproducibility, using the Model 800. Thus, the exceptional performance of this analyzer enables users to consistently meet USP requirements.

This is the ideal response efficiency, indicating the same recovery for both easy-to-oxidize and difficult-to-oxidize substances, and falls well within the range of 85–115% dictated by USP.

References

1. <643> Total Organic Carbon, Pharmacopeial Forum, Jan-Feb. 1996, Volume 22, Number 1, page 1842.
2. Draft of In-Process Revision scheduled to appear in Jan./Feb. edition of Pharmacopeial Forum.
3. Also Quinone, 2.5-Cyclohexadiene-1,4-dione, and 1,4-benzoquinone. This compounds has a molecular weight of 108.09. The theoretical carbon content of this compound is 66.67% (Merck Index Eleventh Ed., 8108)

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