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Comparative analysis of TOC and conductivity analysers as applied to pharmaceutical water analysis.

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Abstract

Pharmaceutical grade water requires the measurement of bioburden, Total Organic Carbon and conductivity. Here we report a comparative analysis from two TOC analysers and two conductivity systems. The TOC analysers showed significantly different results.

Introduction

Pharmaceutical grade water (both purified water and water for injection/irrigation) has a Total Organic Carbon (TOC) limit of 500 ppb. Several commercial companies supply TOC analysers of different designs, however all work on the dual principles of organic oxidation with subsequent measurement of the CO₂ generated. Oxidation can be done using chemical, catalytic, UV irradiation or a combination. Detection systems utilise IR spectrometry or the elevated conductivity of dissolved (aqueous) CO₂. The pharmacopoeial monographs do not stipulate the nature of the oxidation and detection systems, only that a suitable analyser should be able to measure 500 ppb sucrose and benzoquinone standards with reasonable accuracy.

Pharmaceutical grade water also has a conductivity limit to ensure the adequate control of ionic contaminants. Again suitable analysers can be bought from a variety of suppliers, but the measurement systems are fundamentally similar - simply measuring the resistance of a solution across a gap. Temperature measurements are also required since the conductivity of water varies accordingly.

Here we report a comparative analysis for both TOC and conductivity measurements between two different TOC analysers with different configurations. We also analysed pairs of TOC and bioburden results

Materials and Methods

Over 200 samples of purified water and water for injection were split and analysed for TOC using a Hach Lange PAT700 and a Sievers 900. Conductivity measurement were made using the PAT700 and a 'standalone' inoLab Cond 730. For the microbiological analysis over 200 samples of purified water were tested for bioburden and TOC according to the pharmacopoeial monograph

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Figure 1a: TOC sample pairs

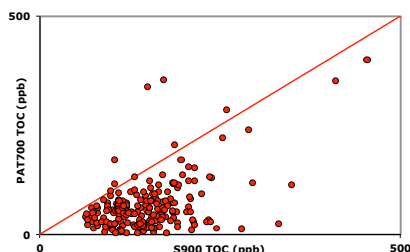


Figure 1b: Conductivity sample pairs

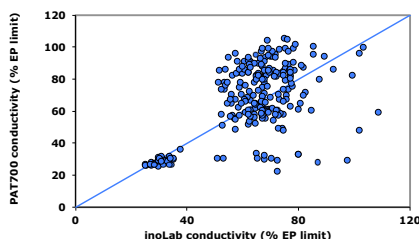


Figure 2: 'Bin analysis' of external/PAT700 ratios

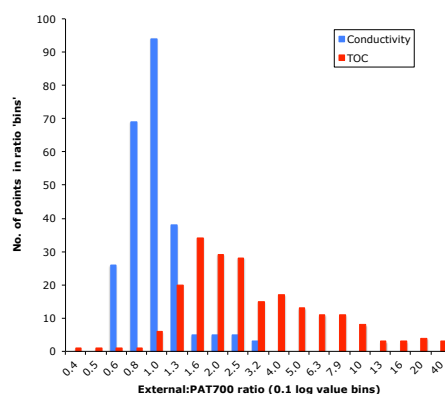
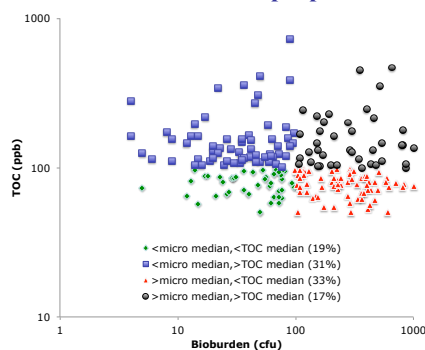


Figure 3: Scatter plot of TOC and bioburden sample pairs



Results and Discussion

Scatter plots of the TOC and conductivity measurements from the samples are shown in Figures 1 a and b (together with the unity gradient lines). To correlate for the effects of temperature the conductivity results are shown as a percentage of the conductivity limit at the measurement temperature according to the pharmacopoeial monograph. The ratios between the two sets of results are plotted as a 'bin analysis' in Figure 2.

The differences between the two TOC analysers are both obvious from the graph and statistically significant suggesting that either experimental artifacts or instrumentation design affects measurement. While the conductivity results are also statistically different, the ratios of the inoLab: PAT700 results are far closer to 1 (see Figure 2), commensurate with two conductivity measurement systems which operate on equivalent principles.

The paired bioburden and TOC results are plotted in Figure 3, as data points above and below the median TOC and bioburden values. The percentages of samples in each class are given in the legend, but the equivalent distribution suggests there is no correlation between measured TOC and bioburden.

A more extensive comparison of the two TOC analysers [1], indicated that while the sucrose and benzoquinone TOC standards are intended to represent organic substances that are 'easy' and 'difficult' to oxidise, they may not adequately represent the variety of organics likely to be found in pharmaceutical grade water (proteins, lipids etc).

Conclusion

This work indicates significant differences between TOC measurements on pharmaceutical grade water samples made using two analysers with different configurations. Both analysers were calibrated according to the pharmacopoeial requirements. Conductivity measurements did not show such pronounced differences. There appears to be no correlation between measured TOC and bioburden levels in purified water.

References

[1] A. Gray, L. Dick, M.A. Elliott, S.J. Ford, G.W. Halbert, (2012) A comparative analysis of two different analysers used for determination of the Total Organic Carbon in pharmaceutical grade water, European Journal of Parenteral and Pharmaceutical Sciences, 17 (2) pp 47-51

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