An Analytical Detector Comparison for TOC Analysis in Cleaning Validation and Water Purification Applications

Product White Paper

Determining the best TOC analyzer for cleaning validation and purified water applications often results in a comparison of the two commonly used detection techniques: NDIR detection and membrane conductivity. In this study, an analytical comparison of these detection techniques was conducted using several different matrices and analytes in a pharmaceutical application.

Background

Conductivity

TOC analyzers that employ direct conductivity detectors offer the simplest and most compact design available. The conductivity method (including direct and membrane conductivity) measures the conductivity of the sample before and after it is oxidized. The resulting differential measurement is attributed to the TOC content of the sample. During the sample oxidization phase, Carbon Dioxide (CO_2) and other gases are formed. The dissolved CO_2 forms a weak acid, thereby changing the conductivity of the original sample in proportion to the TOC content. The success of the technique relies on the assumption that only CO_2 is present in the sample matrix. In the event that other chemical species are present in the sample, their individual products of oxidation may present either a positive or a negative interference to the actual TOC value, resulting in commensurate analytical error. Additionally, measurements over 50 ppmC are not uniformly proportional to the TOC of the sample and therefore not achievable.[1] Lastly, the conductivity compensation errors related to temperature and pH, can also be of significant importance.

Membrane Conductivity

A different approach to improving the accuracy of TOC analysis using conductivity incorporates the use of hydrophobic gas permeation membranes. These membranes allow a more “selective” passage of the dissolved CO_2 gas to the “zero” water used for conductivity analysis. While this approach has solved certain problems, membranes often have their own particular limitations. Potential problems often include clogging, true selectivity, micro leaks, flow problems, dead spots, and microbial growth (blockage). Of greatest concern is the membrane’s tendency to become a location for secondary chemical reactions that promote “false negatives,” a condition far more severe than “false positives”, in critical applications. Because false negatives can lead to an erroneous conclusion of meeting cleaning validation criteria, they are of the greatest consumer safety concerns.

Other concerns include the inability of membrane methods to recover their operational performance after an overload condition arises that over-ranges the instrument. Recovery can often take hours before returning to reliable service and recalibration. Small changes in pH are also a well-known contributor to inaccuracy, leading to incomplete oxidation of organics and consequently CO_2 detection interference.

NDIR Detection

NDIR detectors use Infrared (IR) energy to detect the presence of CO_2. An IR beam is transmitted through the sample chamber as the sample gas containing CO_2 fills the chamber. Pressurized front and rear cells connected by a mass flow sensor are located within the detector. An optical filter allows only light of a predetermined wavelength to reach the detector cells from the IR source. When IR energy passes through CO_2 gas, it creates a unique adsorption spectrum making CO_2 distinguishable from other gases. To collimate the IR light through the sample chamber and to increase optical efficiency, the light source is surrounded by a parabolic reflector assembly, which is typically gold lined.

Any change in gas flow to the cells changes the pressure within each cell individually. This pressure difference is detected by the mass flow sensor, which then emits an electrical signal proportional to the magnitude of the flow. As this occurs, the instrument monitor displays a single point on a graph corresponding to the emitted electrical signal (usually in millivolts [mV]). This point represents the amount of CO_2 inside the detector only at that particular moment. As the adsorption of the infrared light is measured over time, the amount of CO_2 inside the detector increases and decreases as the sample gas flows through the detector. Displayed together, the plotted points relate to the traditional flow-through cell bell-shaped curve. The CO_2 sample result is calculated by the mathematical integration of the area underneath this curve. The NDIR detection technique offers a more practical, interference-free method for detecting CO_2 in TOC analysis. By measuring CO_2 in the gas phase, interference effects of other compounds remaining in the sample are eliminated.[2]

Figure 1 A Comparison of Two TOC Analyzers using Membrane Conductivity vs. NDIR Detection Technology for Analysis of TOC in 0.8% NaCl at Increasing TOC Concentrations. Each Analyzer was Calibrated to its Manufacturing Specifications Prior to Analysis.

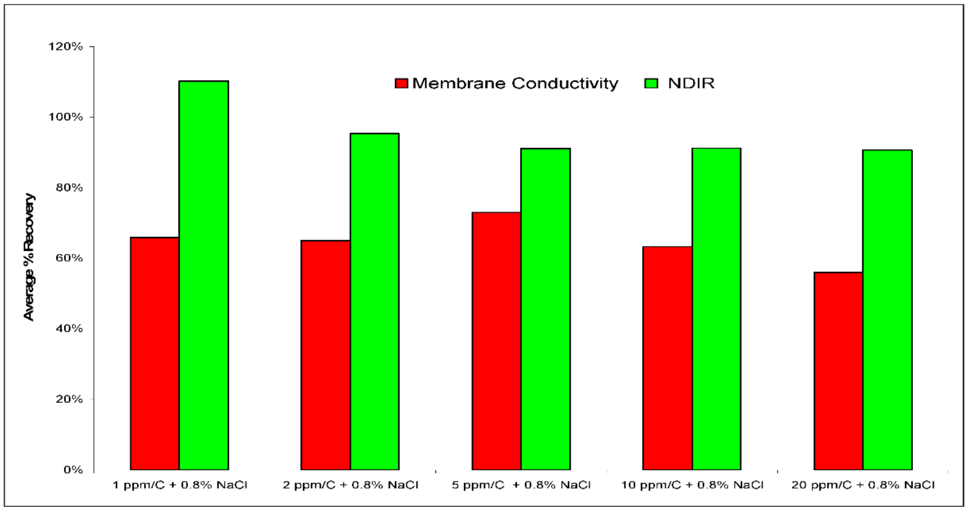


Figure 2 A Comparison of Pharmaceutical Compounds using Membrane Conductivity vs. NDIR Detection Technology.

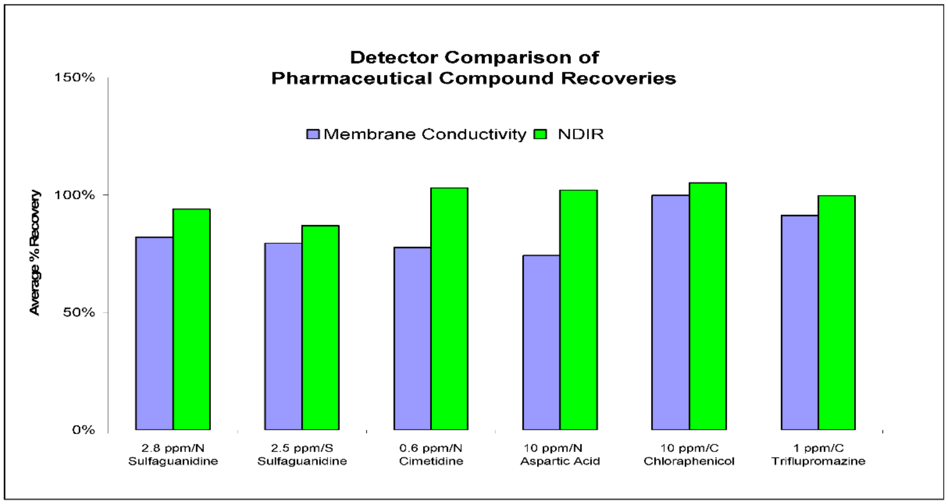


Figure 3 A Detector Comparison of TOC Analysis with Increasing Amounts of Azide Present in an Aqueous Sample.

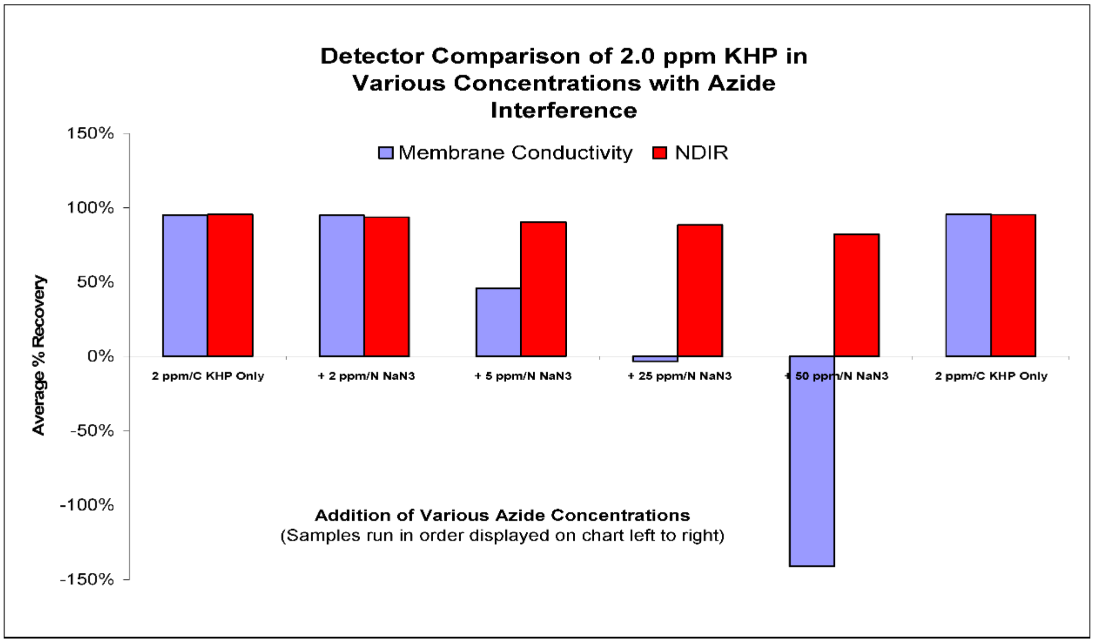
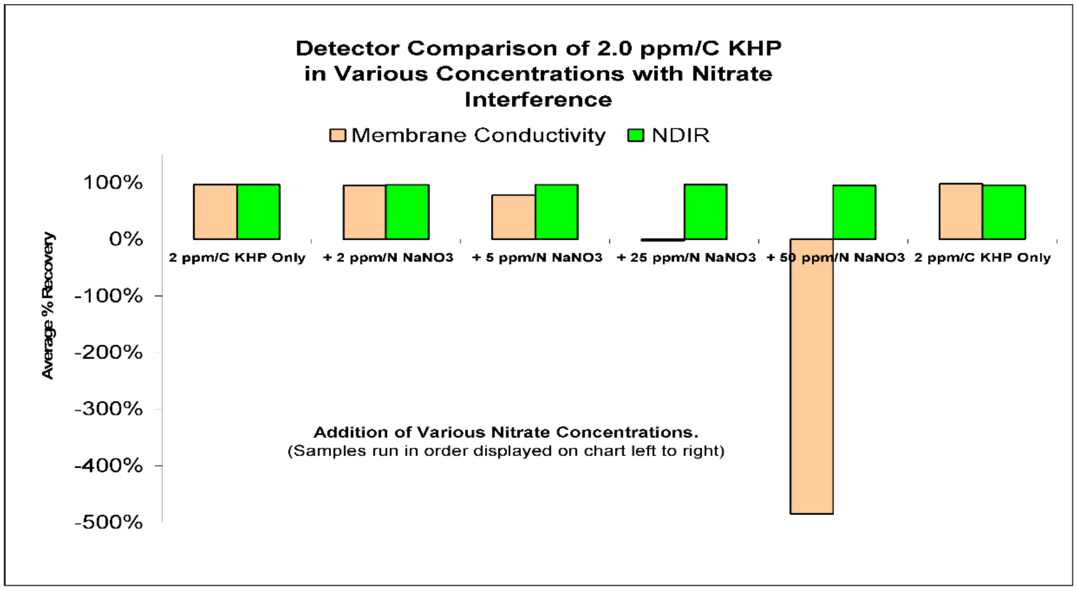


Figure 4 A Detector Comparison of TOC Analysis with Increasing Amounts of Nitrate Compounds Present in an Aqueous Sample.



Conclusion

A comparison of brine sample analysis at a concentration of 0.8% sodium chloride shown in Figure 1, demonstrates the superiority of NDIR detection. NDIR detection far surpasses the ability of membrane conductivity detection to analyze brines. A comparison of hard to oxidize pharmaceutical compounds (due to their complex molecular structure and varying levels of nitrogen, sulfur, and carbon) is shown in Figure 2. As illustrated, the membrane conductivity detector did not effectively recover these compounds in comparison to the NDIR detector. Figure 3 and Figure 4 demonstrate the nitrogen chemical species in the sample (and their individual oxidation products) interfering negatively with the membrane conductivity TOC recovery, as the nitrogen concentration increases. NDIR detection technology achieved superior recovery and accuracy over membrane conductivity for all compounds analyzed, as well as a wide range of sample water matrices.

References

1. Light, T.S.; Kingman, E.A.; Bevilacqua A.C. *The Conductivity of Low Concentrations of* CO_2 *Dissolved in Ultrapure Water From 0-100 °C*; Paper presented at the 209th American Chemical Society National Meeting, Anaheim, CA, April 2-6, 1995. [Online] http://www.gatewayequipment.com/cond_CO2.pdf (accessed Sept 28, 2017).
2. Wallace, B.; Stevens, R. Evaluating Oxidation and Detection Technologies, *Pharmaceutical Formulation*. March/April 2004, 76 – 77.