BALAZS™ nanoanalysis

Water Analysis

Speciation of Organic Compounds in Pharmaceutical Process Waters

Regulation of pharmaceutical waters ensures high quality and safe water for production processes. However, the possibility of organic compounds present in filtration feed water or leached into production water can pose serious problems for purification steps, process applications, and product manufacturing. The presence of high levels of natural organic matter (NOM) may cause numerous problems:

- Compliance issues may arise if TOC limits are not met (TOC limit for pharmaceutical waters is 500 ppb)
- High molecular weight organic compounds may cause filter fouling during purification
- Organic material present may indicate bacterial growth

Purification and manufacturing issues caused by contaminated waters will likely be complicated and costly to resolve without knowledge of the source of the problem. However, many methods for measurement of organic compounds are limited in the efficiency and specificity of their analyses. Some methods are very specific for identification of certain compounds, but limited in their ability to detect others.

Organic Speciation using LC-OCD

Balazs™ Nanoanalysis offers organic speciation using liquid chromatography-organic carbon detection (LC-OCD) which provides an effective analysis of organic compounds within the tested water. This method allows for identification of biopolymers, humics, low molecular weight (LMW) acids, volatile organic compounds, and more, while characterizing nearly 100% of the organic composition. LC-OCD is a non-target complementary method to existing target methods for detection of synthetic compounds. When accurate determination of specific compounds is required, more specific techniques may need to be used. LC-OCD analysis can help design treatment systems, monitor changes in water quality, and define solutions for a large array of problems without the need for expensive specialized tests.

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AIR LIQUIDE ELECTRONICS

Case Study

Obtaining a DOC level under the target (500 ppb) for pharmaceutical water for injection (WFI) is relatively simple. However, the LC-OCD method can give a beneficial analysis of the components within the tested water. In this case, ammonium and urea are present in WFI A and B. A qualitative analysis of the organic contents in the process water can facilitate the solution to many issues that are present within the treatment process.

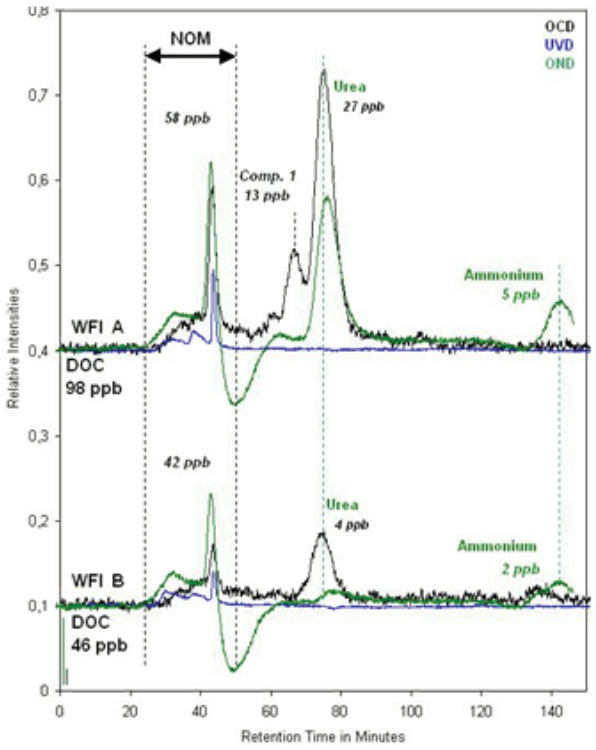

Figure 1. Analysis of water for injection in pharmaceutical applications

LC-OCD Method Overview and Definitions

The LC-OCD process begins with the injection of a small sample into a size exclusion chromatography column where high molecular weight (HMW) compounds are separated from LMW compounds. The sample is then fed to UV and organic nitrogen detectors, where all compounds containing nitrogen will be analyzed. A UV thin film reactor serves as the heart of the process where organic compounds are oxidized producing carbon dioxide, whereas the originally present CO_2 is removed through acidification and N_2 sparging. The resulting CO_2 is measured using a non-dispersive infrared detector (NDIR). The output of this analysis is a report containing the chromatogram (see Figure 2) and the spreadsheet providing organic speciation to the following content:

DOC – Dissolved Organic Carbon
DON – Dissolved Organic Nitrogen
HOC – Hydrophobic Organic Carbon (organic compounds that do not elute during the period of time of the test)
CDOC – Chromatographic (hydrophilic) Dissolved Organic Carbon (organic compounds that elute completely during the period of time of the test)
NOM – Natural Organic Matter
SOM – Synthetic Organic Matter > 10 ppb

Quantification and Characterization of:

- Humics,
- Biopolymers,
- Building Blocks,
- LMW-acids

In addition to the above categories, specific organic compounds are identified based on the instrument library, characterized by chromatography retention time, nitrogen content, and presence of unsaturated bonds (identified by UV detector). Balazs™ also includes interpretations help for practical conclusions.

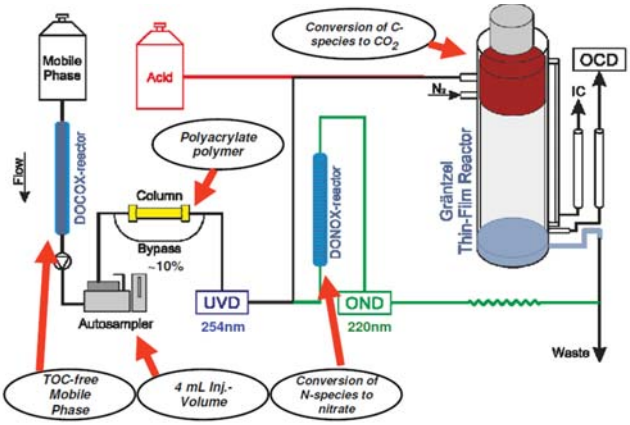

Figure 2. LC-OCD schematic diagram

References

- Huber, S.A.; Balz, A.; Abert, M., Pronk, W.: Characterisation of aquatic humic and non-humic matter with size-exclusion chromatography - Organic Carbon Detection - Organic Nitrogen Detection (LC-OCD-OND). Water Research 45 (2011), 879-885.
- Huber, S.A., Balz, A., Abert, M.: New method for urea analysis in surface and tap waters with LCOCD-OND (liquid chromatography-organic carbon detection-organic nitrogen detection). Aqua, 60.3, (2011), 159-165.
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