A New HPLC Detector

Utilizing Condensation Nucleation Technology

NQAD™

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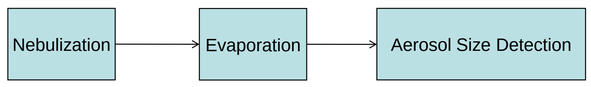
Abstract:

A new aerosol-based HPLC detector using condensation nucleation has been developed to provide high sensitivity and a wider linear range than existing aerosol-based HPLC detectors by Quant Technologies of Blaine, MN, USA.

- Overview of aerosol based detectors
- What is NQAD, how does it work, why it was developed
- Operating Requirements
- For what types of analyses is the NQAD useful
- Some sample data

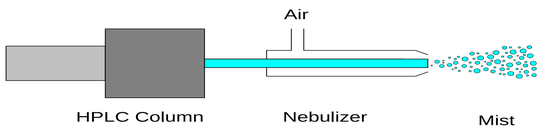
How Aerosol Based Detectors Work:

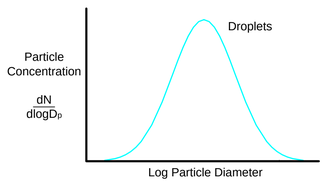


ELSD – Light Scattering

CAD – Charge Acceptance

NQAD – Particle Counting



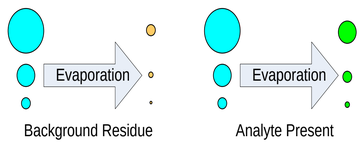


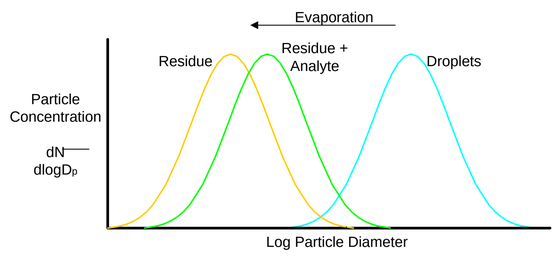
Nebulized Aerosol Distribution
• Log Normal
• Stable

How The NQAD Detects An Analyte:

The NQAD utilizes a particle counter that selectively grows particles by condensation of water vapor.

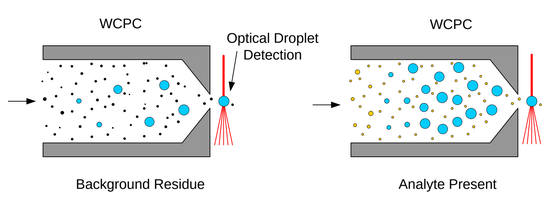
•Droplets evaporate leaving particles made up of non-volatile residue
•As the level of non-volatile residue increases the size of the particles increases.





•Only particles larger than a threshold size grow to be large enough for optical detection

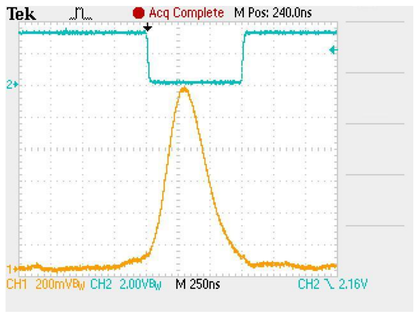
•Particles that do not grow remain too small for optical detection



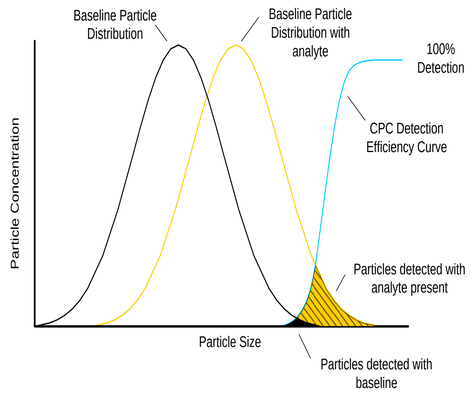
Aerosol Size Detection

The NQAD converts the particle count rate into a chromatogram output signal. By measuring the nebulized aerosol using this technique very small shifts in the size of the aerosol distribution can be measured. To the analytical chemist this translates to high sensitivity analyte detection. Unlike other aerosol based detectors there is no interference from sensor noise or drift that can interfere with resolution and sensitivity.

- Very high signal to noise ratio – allows for ultrasensitivity and stability.



WCPC Detection Efficiency Curve
• Stable



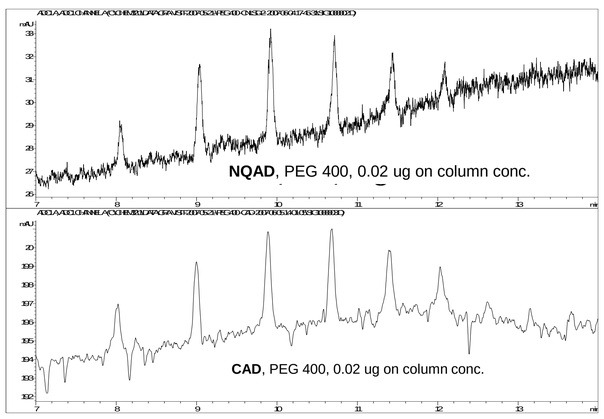
What is new with the NQAD?

- Enhanced semi-volatile analyte detection
- Increased data rate
- Ethernet capability

Performance:

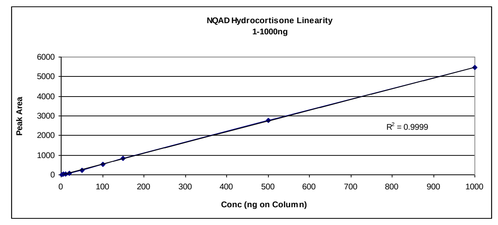
Sensitivity:

For many analytes the NQAD has limits of detection that are 1ng or less. Reducing the level of background non-volatile residue can further increase the sensitivity of the detector. A technique similar to NQAD is used in the ultra pure water industry where instruments are able to detect changes in residue < 10 part per trillion (3). The following shows compares the sensitivity of the NQAD compared to other commercially available aerosol based detectors.



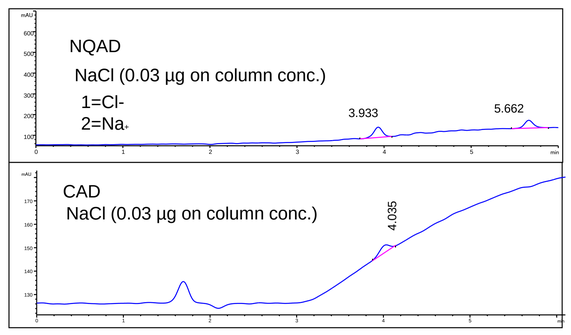
Linearity and Dynamic Range:

Several factors influence the linearity and dynamic range of aerosol based detectors. It is important to consider that for analyses that have a high background of non-volatile residue the overall dynamic range will be reduced and the linearity can be affected. The following chart shows an example of hydrocortisone linearity and dynamic range.



Stability / Reproducibility:

Performance testing of the NQAD has shown the detector generally has reproducibility of 5% RSD or better. The stability of the baseline for gradient analysis has been a problem with aerosol based detectors. Testing of the NQAD has shown good baseline stability and repeatability and reduced baseline drift during gradient analysis when compared to other commercially available aerosol based detectors. The following plot is a comparison between NQAD and CAD with a gradient analysis. The arrows indicate a change in the mobile phase composition.



Conclusion:

There are several advantages of aerosol based HPLC detectors over other traditional HPLC detection techniques. The majority of common HPLC detectors are not considered universal in the sense that a specific property of the analyte is required for the detector to work e.g. a requirement for a chromophore containing analyte for UV detection. The limitation for aerosol based detectors is that the analyte must be non-volatile although many semi-volatile compounds are also detectable. Otherwise aerosol based detectors are considered to have universal detection. Additionally there is no difficulty using gradient methods as is the case with refractive index (RI) detectors. Aerosol based detectors in general have good sensitivity (low ng to 100ng) and are cost effective.

Evaporative Light Scattering Detection (ELSD) is a common aerosol based HPLC detector that has been commercially available for several decades. The principle of ELSD is to measure the change in the amount of light scattered by the aerosol using a light source and photodetector. As the size of the aerosol increases the amount of light scattered by the aerosol increases which is then converted into a signal. The sensitivity of ELSD detection typically ranges from 10 to 100ng.

A more recent type of aerosol based detector is based on measuring the ability of the aerosol to accept a charge. The larger the particles in the aerosol are the more charge they will accept. An electrometer measures the aerosol charge and converts it into a signal. This type of instrument is referred to as a Charged Aerosol Detector (CAD).

The disadvantage of both the ELSD and CAD is their use of direct signal measurement from their sensor. This type of measurement has inherent sensor noise and drift that limits the sensitivity and stability of the overall detector.

The Quant Technologies NQAD is the first commercially detector using the condensation nucleation technology measurement technique. When using the detector for high sensitivity analysis the chemist must consider sources of non-volatile residue that may interfere with the analysis. The detector has proven to have sensitivities at least as sensitive and in many cases much higher sensitivity than other commercially available aerosol based detectors.

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The patented WCPC technology is licensed from Aerosol Dynamics, Inc. US Patent # 6,712,881
Other patents pending

References:

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