

Evaluation and Comparison of 3 Common HPLC Detectors for Use in Stability-Indicating Analytical Methodology of Small Molecule Pharmaceuticals

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1 PURPOSE

- To examine the potential differences among three typical HPLC detectors when developing and utilizing a stability indicating method for the identification of potential impurities and degradants when conducting non-clinical dose formulation analysis of a small molecule active pharmaceutical ingredient (API).
- The three types of detection examined are: ultraviolet (UV), diode array (DAD), and charged aerosol detection (CAD).
- This poster will demonstrate the benefits of each HPLC detector while also demonstrating the potential limitations when using the listed detectors when optimizing a stability indicating method

2 METHODS

- A Dionex Ultimate 3000 HPLC coupled with a Dionex Corona CAD and a ultra-violet (UV) detector was used for the quantitation of the degradants of 2 standard APIs.
- An Agilent 1100 HPLC coupled with a diode array detector (DAD) was also used for the quantitation of the degradants of 2 standard APIs.
- Separation was achieved with a standard C18 column using a shallow gradient from 95% aqueous mobile phase: 5% organic mobile phase to 5% aqueous mobile phase: 95% organic mobile phase with potential acid modifiers.
- Degradation of the 2 standard APIs was achieved by exposing the compound to heat (> 60°C) as well as addition of a strong acid, monitoring the increase in degradants over time.
- Data acquisition and analysis were performed using Dionex Chromeleon® software version 6.8.

3 RESULTS

- The CAD demonstrated the most versatility with the ability to detect any impurities and degradants with a response greater than the baseline noise. However, the detector does not demonstrate the sensitivity of a UV detector
- The UV detector demonstrates great selectivity and sensitivity, especially when the method is specialized for the detection of the API. However, the limitation of utilizing a single wavelength to detect any impurity/degradant peaks while analyzing for the API may lead to a false sense of the impurity/degradant content
- The DAD offers the same sensitivity and selectivity of a UV detector, but it has the capability to monitor more than one wavelength
- However, any impurities and/or degradants that lack a chromophore could not be detected during the analysis using UV or DAD

4 CONCLUSION

- The CAD demonstrated the most versatility with its ability to detect specific degradants along with their impurities with a response greater than the baseline noise and reproducible results. However, CAD is less sensitive than an UV detector.
- The UV detector cannot identify all the impurities and degradants simultaneously
- Proper consideration of the analytical column as well as system parameters and conditions impact the development of the stability-indicating method as much as the detector settings

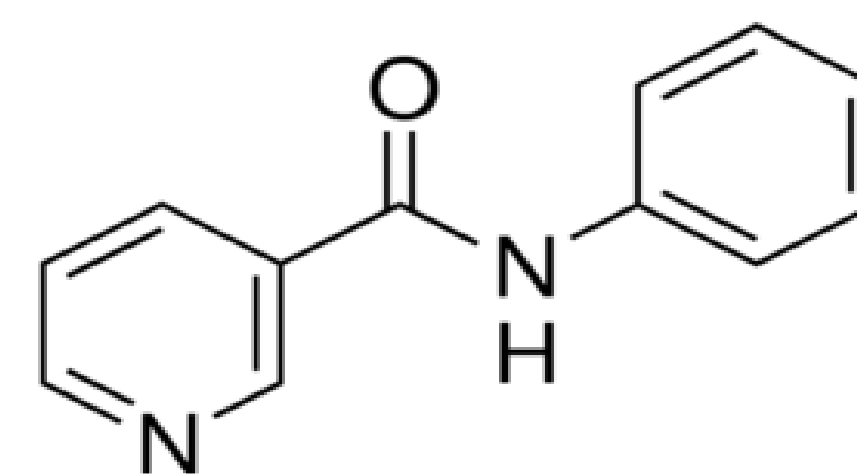


Figure 1. Nicotinanilide

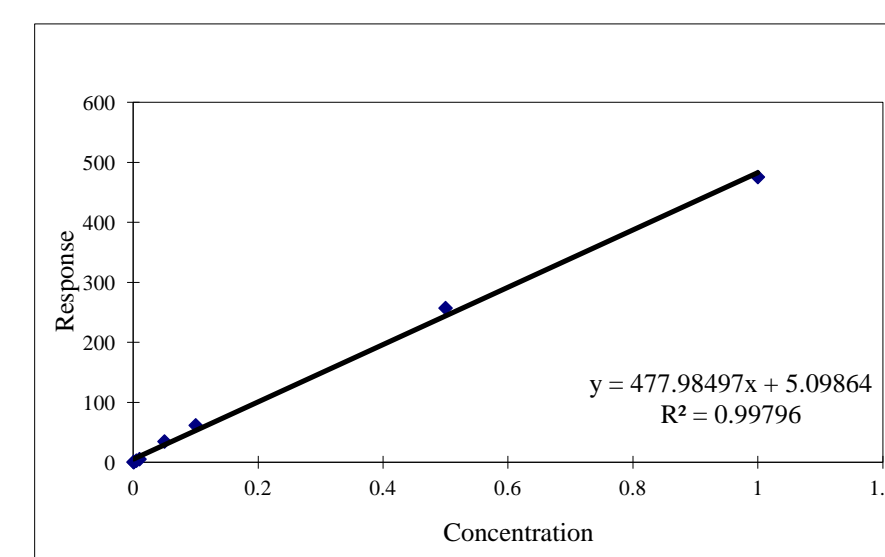


Figure 2. Nicotinanilide calibration curve

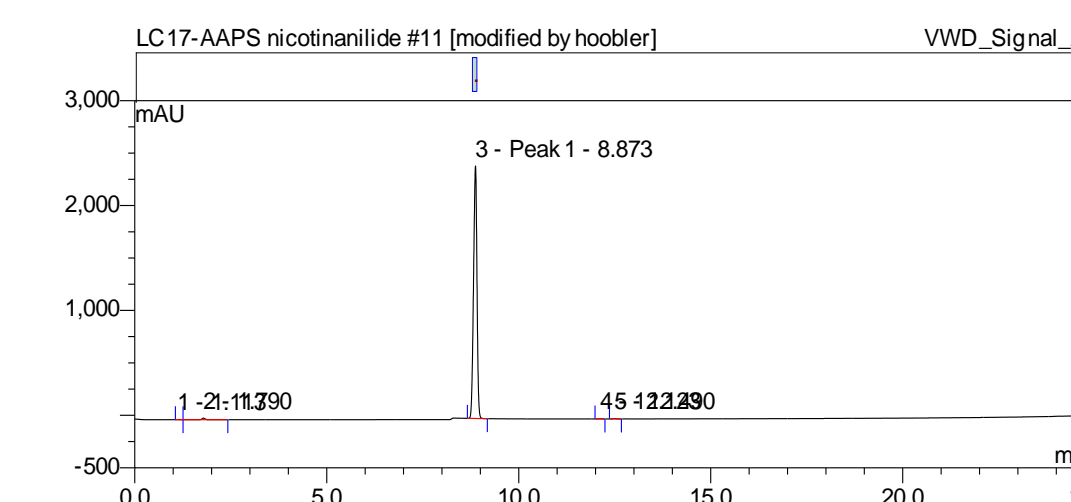


Figure 3. Nicotinanilide standard 0.5 mg/mL - UV

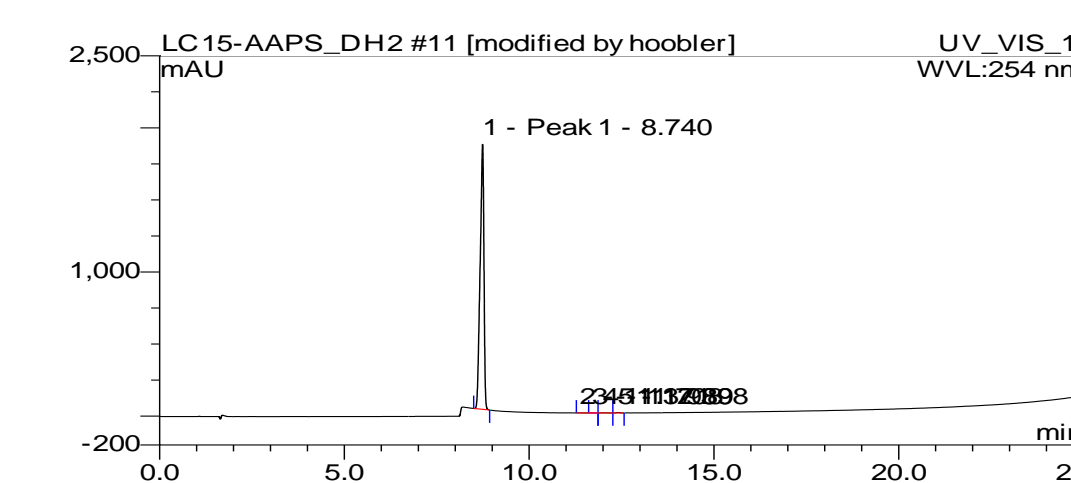


Figure 4. Nicotinanilide standard 0.5 mg/mL - DAD

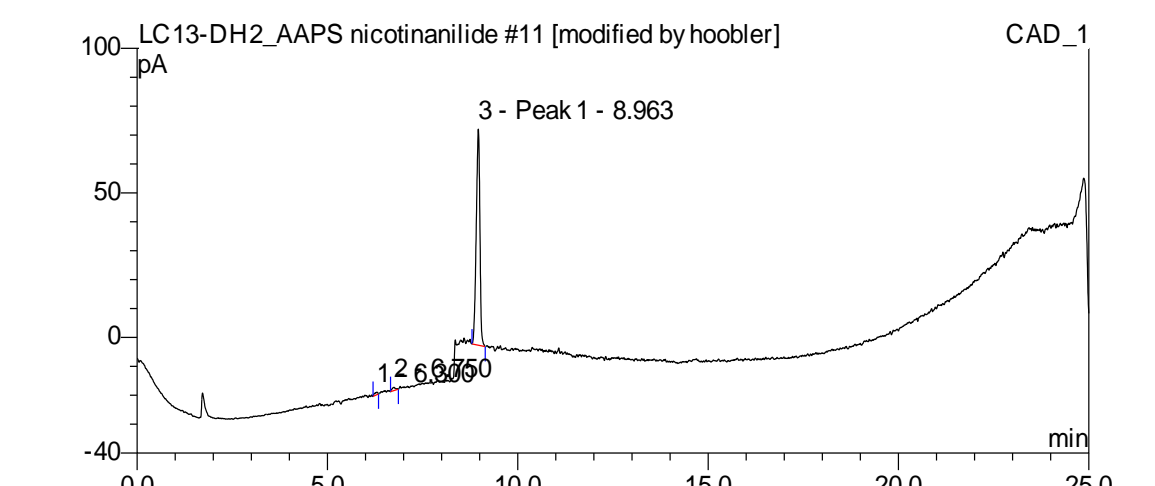


Figure 5. Nicotinanilide standard 0.5 mg/mL - CAD

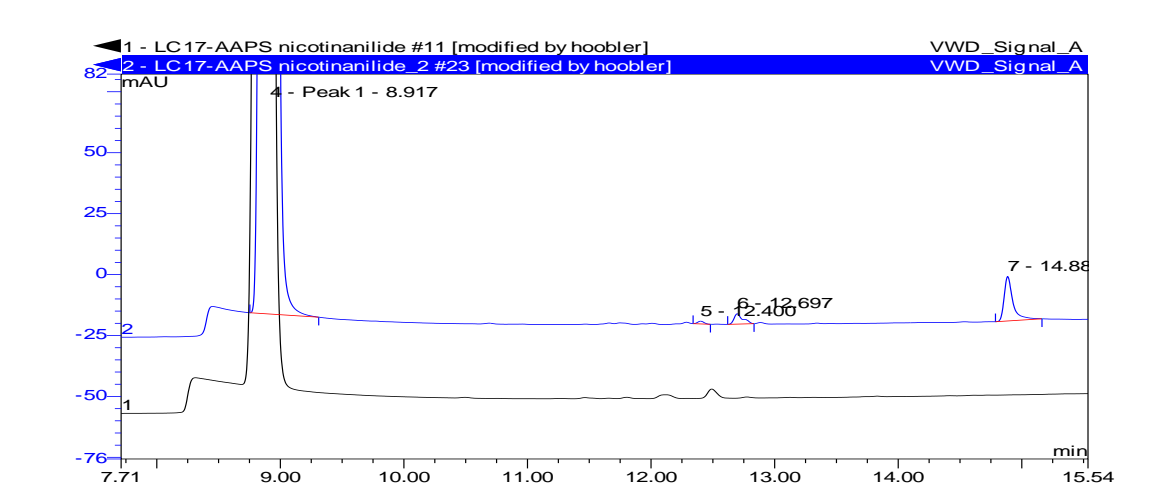


Figure 6. Nicotinanilide standard 0.5 mg/mL degraded after 6.5 hours @ 65°C