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Optimization of UV Detector Parameters of Compendial Methods

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PURPOSE

Within the pharmaceutical industry, compendial LC methods are used to assess product safety and efficacy. These methods often use UV detection for analysis. Aside from the detector type, the methods specify the UV wavelength(s) required for the analysis but do not provide any further information regarding other detector parameters. Due to this, default UV detector settings are frequently used. While these default settings might produce acceptable chromatography, for challenging methods modifications may be needed to meet the system suitability requirements defined in the method. An understanding of available UV detector parameters, including settable and default values is important to produce optimal chromatography.

This study describes a process to evaluate and optimize the detector parameters used for a USP method.

METHOD(S)

The USP method for organic impurities in ibuprofen tablets was studied. The method's system suitability requirements include a signal-to-noise ratio (s/n) of not less than (NLT) 10 for a 5-ppm solution of ibuprofen. The signal-to-noise ratio, a measure of the UV signal for the ibuprofen peak relative to the background noise, was used to define method sensitivity.

METHOD: USP Ibuprofen Organic Impurities (Isocratic Reversed Phase Separation)	
Mobile Phase	4 g/L chloroacetic acid in 40:60 Water:Acetonitrile, pH 3
Flow Rate	2.0 mL/min (isocratic)
Run Time	10 minutes
Injection Volume	10.0 µL
Column Temperature	25.0 ºC
Sample Temperature	15.0 ºC
Column	XBridge™ BEH C18 column: 4.6 x 250 mm, 5 µm (P/N 186003117)
Detector	UV: λ = 254 nm (10 mm flow cell)
Seal Wash	10:90 Acetonitrile: Water
Needle Wash	90:10 Methanol: Water

The system suitability solution was initially analyzed using a PDA detector having all parameters (except for wavelength) set at default values. Individual detector parameters were changed and optimized based on their impact to the signal-to-noise ratio. The system suitability solution was re-analyzed using the optimized settings and the results compared against those obtained using default values.

REFERENCES

1. Monograph: USP. Ibuprofen Tablets. In USP-NF. Rockville, MD: USP; Dec 1,2016. DOI: https://doi.org/10.31003/USPNF_M39890_01_01
2. L. Gauthier, P. Hong, *Optimization of Detector Parameters to Improve Sensitivity using the Alliance™ iS HPLC System with PDA Detector*, Waters Application Note, 720008901

RESULT(S)

Initial testing of a 5-ppm ibuprofen solution at 254 nm using default detector settings failed to meet the required signal-to-noise ratio (≥10). To improve performance, key parameters—data rate, filter response, slit width, optical resolution, and absorbance compensation—were individually adjusted to assess their impact on s/n.

The **data rate** defines the rate that the detector collects data. The optimum data rate was 2 Hz. A data rate of 2 Hz produced a well-defined ibuprofen peak with 31 data points (within the target range of 25–50) and reduced noise compared to the default. This resulted in a signal-to-noise ratio of 25, meeting system suitability criteria.

With the data rate set at 2 Hz, the detector's **filter response** was examined. This parameter controls a high frequency noise filter. The optimized filter response was 2 seconds. Adjusting the filter response from the default setting of 1 sec to 2 sec increased the signal-to-noise ratio from 25 to 33.

The **optical resolution**, which determines the number of diode responses that are averaged in calculating absorbance at the specified wavelength, was also examined. Changing the optical resolution from its default value of 4 nm had little impact on the signal-to-noise ratio, so the default value was retained.

The **slit width** setting controls the amount of light that reaches the photodiode array sensor. For this method, altering the slit with from the default (50 µm) did not significantly change the signal-to-noise ratio therefore, the default value was kept.

Absorbance compensation improved the signal to noise ratio by reducing non-wavelength dependent noise. Using this feature, the average baseline absorbance from a non-absorbing wavelength range was subtracted from the absorbance of the ibuprofen peak. Enabling this feature increased the s/n from 33 to 51 - a 1.5 x gain in sensitivity.

Finally, the optimized settings were combined and the signal-to-noise ratio re-measured. The result was compared against that obtained using default values. The signal-to-noise ratio increased from 7 to 51 surpassing the NLT 10 requirement.

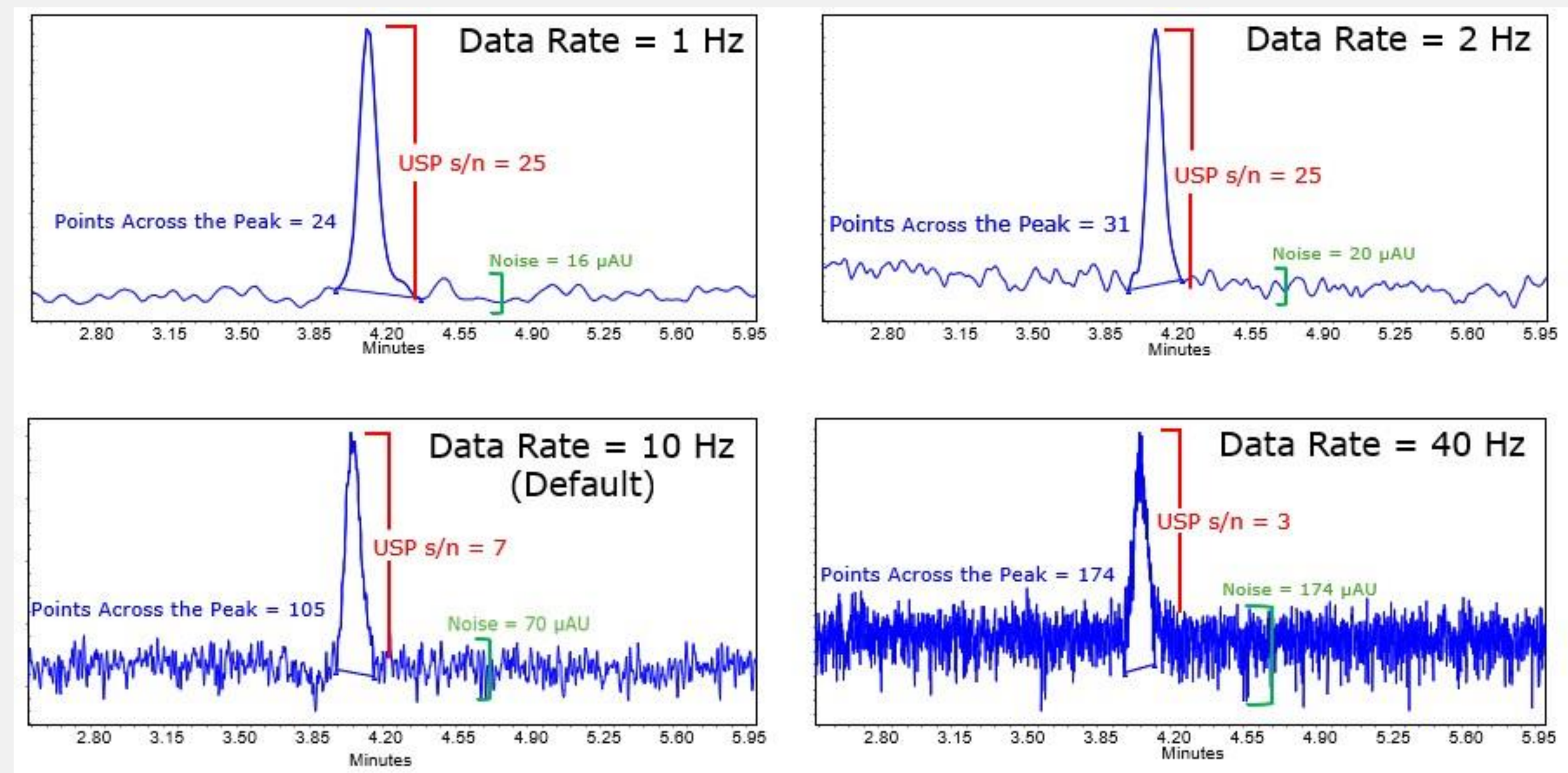

Figure 1: Impact of Data Rate

	PDA Settings					Results	
	Data Rate (Hz)	Filter Response (sec)	Resolution (nm)	Absorbance Compensation	Slit Width (µm)	Noise (µAU)	USP s/n
Default	10	1 (Normal)	4	Off	50	70	7
Optimized	2	2 (Slow)	4	On (310 -410 nm)	50	8	51

Table 1: Comparison of results using default and optimized settings

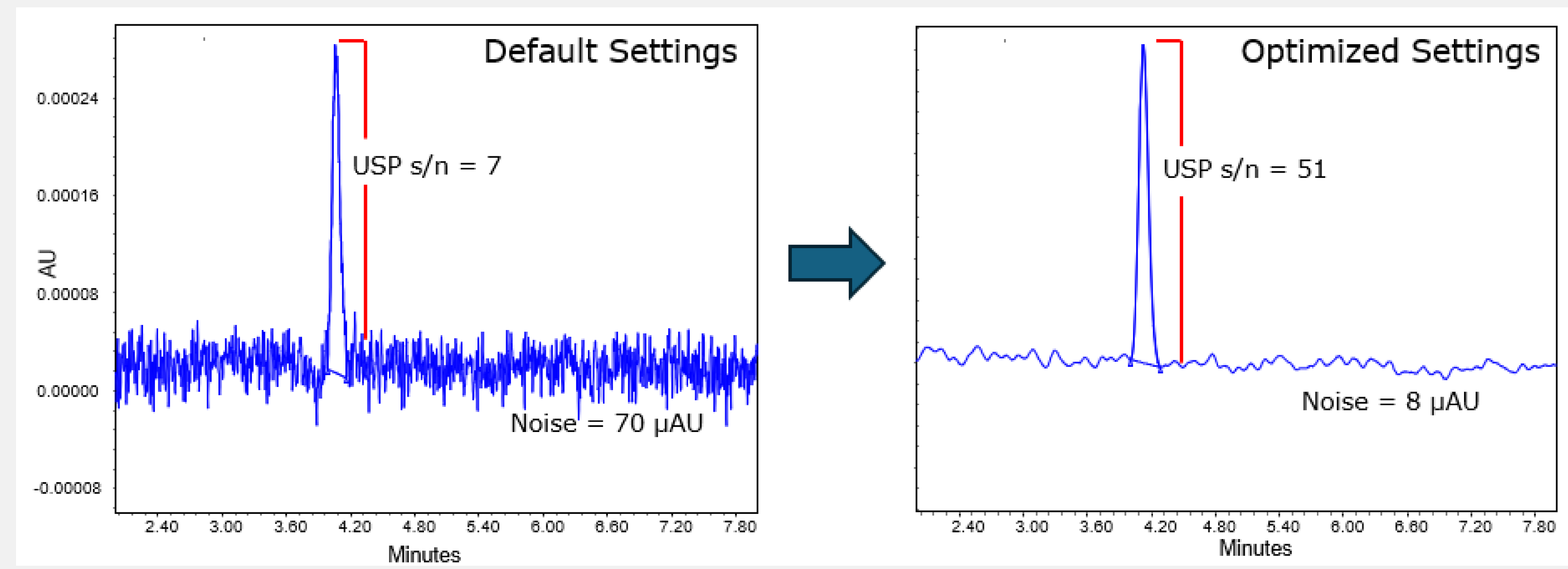

Figure 2: USP s/n with default and optimized detector settings

CONCLUSION(S)

Default UV detector settings are generally suitable for routine HPLC, but they may require adjustment for more demanding methods. The influence of detector parameters on method performance was evaluated using the USP method for organic impurities in ibuprofen tablets. When executed on a photodiode array (PDA) detector under default detector settings the method failed to meet the system suitability requirement for signal-to-noise ratio (s/n). Key detector parameters were systematically evaluated and optimized:

- Data rate had a significant impact on s/n
- Increasing the filter response to 2 seconds improved s/n
- Absorbance compensation boosted sensitivity by 1.5 X
- Optical resolution and slit width had minimal effect and were kept at default

Implementation of the optimized settings resulted in a sevenfold increase in sensitivity, which easily meets the s/n requirement. The study highlights the importance of reviewing, understanding, and optimizing UV detector settings for meeting system suitability and improving sensitivity.

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