Extending the Linear Dynamic Range of Photo Diode Array Detector

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Summary

A new data processing method for a photo diode array (PDA) detector achieves 10 times wider linear dynamic range.

When peak integration of data acquired with a PDA detector exceeds a certain threshold, the method shifts the spectrum to a lower UV absorption wavelength automatically. It then determines the peak and area from the acquired chromatogram, corrects the absorption ratio between wavelengths using the spectrum information, and calculates the peak area and height of the target wavelength. It is applied to the pharmaceutical sample Ofloxacin.

Following the test procedure in the pharmacopeia, sample dilution is needed to determine the high-concentration component and the low-concentration related substances. However, in the dilution process, there is a risk of human error. This risk is avoided if all peaks are quantified by a single injection data.

The new method is available to record the evidence that the sample is properly diluted in a regulated laboratory. In this study, the results are compared between the original method and the new method to show the difference in the major component area values is less than 0.1 %.

What is the new method of Dynamic Range Extension, *i*-DReC ?

The *i*-DReC (Intelligent Dynamic Range Calculation) is a powerful technique that expands the dynamic range in cases where a wider range is required, such as for simultaneous quantification of a low abundant impurity with a major target compound. This technique works based on the spectrum obtained using a Photo Diode Array Detector, such as the SPD-M30A/M20A, by shifting the spectrum wavelength when the linearity of the calibration curve cannot be obtained due to intensity saturation of the detector.

When dilution is required due to the limitation of the dynamic range, this function avoids the need for dilution with its extended dynamic range and provides improved work efficiency.

Concept of the *i*-DReC

Conceptual illustration of the *i*-DReC is shown in Figure 1. Although the saturated peak, such as four AU intensity, causes a limitation of its dynamic range, a peak shift algorithm can simulate the net intensity of the peak based on the sensitivity factor shown in the Figure. Wavelength shifted for calculation is defined automatically by software in terms of the set intensity of the correction wavelength.

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• Sensitivity factor is fixed at any concentration
• Saturated peak area (*Aa*) can be calculated using the value of unsaturated area (*Ab*) and sensitivity correction factor (*k*).

Target peak area (*Aa*)
= Peak area extracted different wavelength (*Ab*) × Sensitivity factor (*k*)

High-concentration peak loses linearity and saturates near 4 AU.

Sensitivity Factor

$$k = \frac{\text{Peak height of } Aa}{\text{Peak height of } Ab}$$

ex : 272 nm
Target area=*Aa*
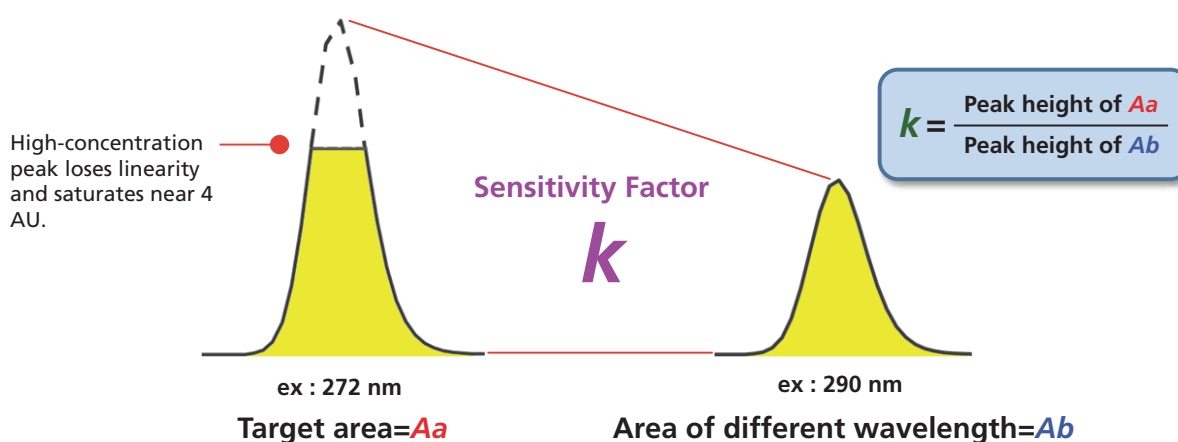
ex : 290 nm
Area of different wavelength=*Ab*

Figure 1: Conceptual illustration of the *i*-DReC

How to Calculate the True Peak Intensity

Figure 2 (a) indicates an example of a saturated peak. First, the spectrum of the peak top is confirmed as shown in Figure 2 (b). The intensity is saturated at the maximum wavelength (*λa*), so obtain an extracted chromatogram at a wavelength (*λb*) which is not saturated.
The peak area in the extracted chromatogram is defined as *Ab* in this example.
Second, an unsaturated extracted spectrum is obtained for sensitivity correction at a time when its intensity is not saturated as shown Figure 2 (c).
In this case, the sensitivity correction factor is defined as *k*, which can be calculated as below.

k = Ia / Ib

If the intensity of the peak is not saturated, its peak area (*Aa*) can be calculated as below.

Aa = k x Ab = Ia / Ib x Ab

By utilizing spectrum similarity in a single peak and conducting corrected calculation of area in a high-concentration region, extension of linearity to high-concentration regions is achieved.

The peak top of λmax chromatogram is saturated, so an accurate calculation cannot be obtained.

λa=240 nm

Area: *Aa*

X

(a) Chromatogram in which there is a saturated peak at λa wavelength

(c) Chromatogram and extracted spectrum at a time which is not saturated

mAU
4000
3000
2000
1000
0

λa   λb   nm

λb=270 nm

Ab

Obtain an extracted chromatogram at a wavelength which is not saturated.

(b) Spectrum of the peak top and chromatogram at λb wavelength which is not saturated

X

Ia

Ib

$k=Ia/Ib$

λa   λb
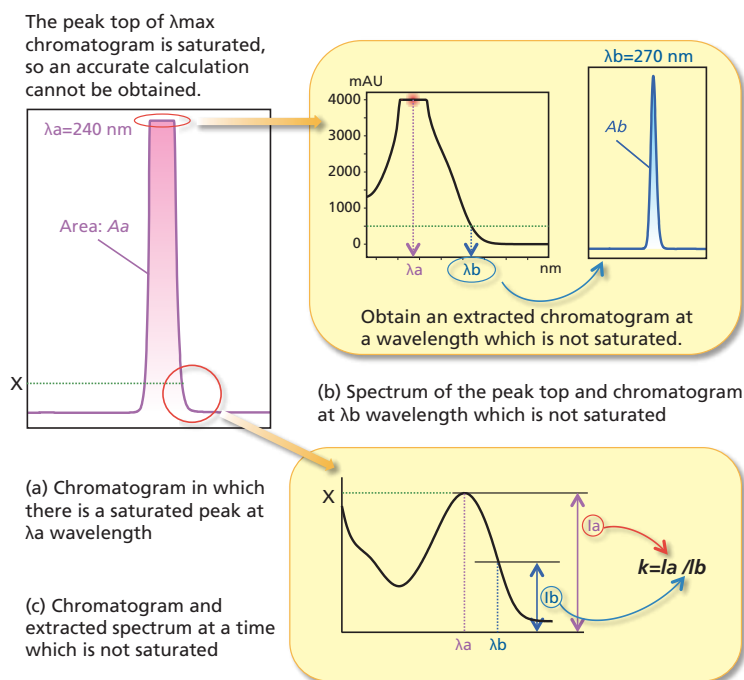
Figure 2: How to calculate the true peak intensity by *i*-DReC

[Features of the *i*-DReC function]

- Simultaneous analysis from low concentration to high concentration in just one injection.
- Easy setting because the wavelength shifting can be automatically defined.
- No need to consider the difference between instruments, such as different optical paths, nor the difference between analyses, such as dilutions, because corrective calculations are done with one data set.
- Superior performance delivered by high-resolution spectrum and noise reduction of the SPD-M30A.

Application of the *i*-DReC
Extension of Dynamic Range for Impurity Analysis

An example of the linearity range extended in a high-concentration sample is demonstrated in this section.
For low abundant impurity analysis, the ratio of the impurity's peak area against the main peak is difficult to obtain due to the dynamic range limitation.
This is a typical example of impurity analysis for a pharmaceutical compound.
For Ofloxacin, a new quinolone antimicrobial agent, several impurity peaks on the chromatogram were observed.
However, although some peaks can be detected in only high-concentration solution, its main peak is saturated.

Normally dilution should be required in this type of case to obtain the correct ratio of peak intensity.
Table 1 shows the result of the peak ratio calculated directly and by the *i*-DReC function without any dilution procedure.
It shows that even from the 10,000 mg/L solution data, the true peak ratio can be obtained by the *i*-DReC function according to the comparison of the results of impurity D, which can be detected in both the low and high concentration of the solution
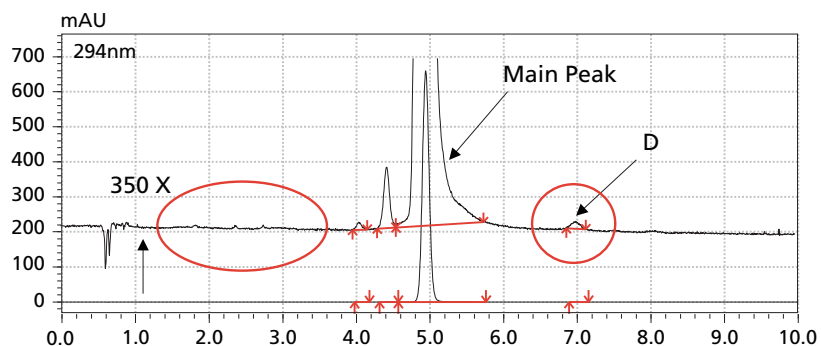
Figure 3 (a): Low concentration of Ofloxacin in solution (200 mg/L)
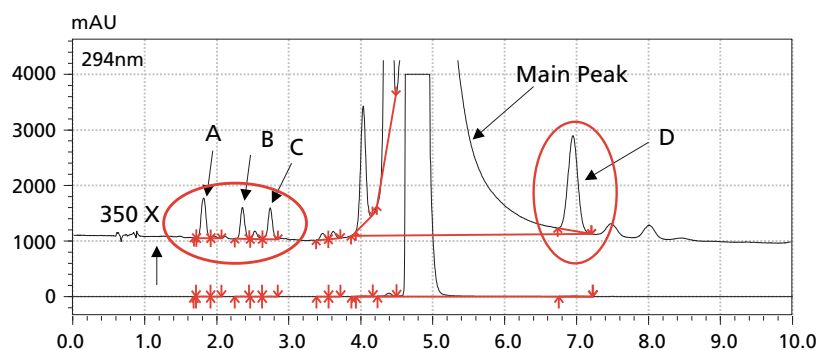

Figure 3 (b): High concentration of Ofloxacin in solution (10000 mg/L)

Table 1: Peak ratio obtained w/ and w/o *i*-DReC function
With a direct calculation, the peak ratios were twice or three times overestimated than with the *i*-DReC's calculation.

		Impurity A	Impurity B	Impurity C	Impurity D	Main Peak
200 mg/L Solution	Peak Area	Not Detected	Not Detected	Not Detected	783	4,213,316
	Ratio (vs. Main Peak)				0.018%	
10000 mg/L Solution	Peak Area (Overestimated)	11,352	7,693	8,254	55,337	91,222,815
	Ratio (vs. Main Peak)	0.012%	0.008%	0.009%	0.061%	
10000 mg/L Solution (*i*-DReC)	Peak Area	11,352	7,693	8,254	55,337	243,307,718
	Ratio (vs. Main Peak)	0.005%	0.003%	0.003%	0.023%	

Table 2: Peak heights obtained w/ and w/o *i*-DReC function
According to the obtained peak heights (mAU unit), dynamic range can be expanded more than 20 AU.

	Peak Height	Peak Height (w/ *i*-DReC)
200 mg/L Solution	657.4 mAU	657.4 mAU
5000 mg/L Solution	4000.3 mAU (Saturated)	11,371.5 mAU
10000 mg/L Solution	4000.0 mAU (Saturated)	20,651.8 mAU

The chromatograms of Ofloxacin sample were obtained under the modified condition described in Japanese Pharmacopeia. The column used was Shim-pack XR-ODS 3.0 x 75mm (Shimadzu) with reversed phase elution.

Simultaneous Determination in Wide Dynamic Range

Another example is described for simultaneous determination for ingredients in a vitamin drink. Several compounds are contained from low to high concentration.
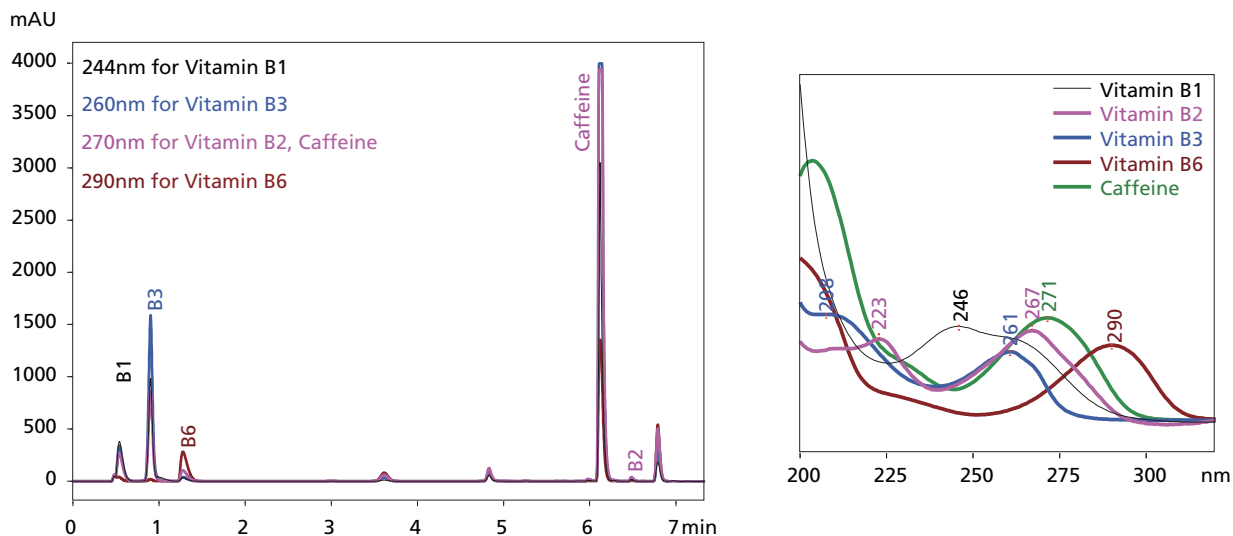

Figure 4: Overlapped chromatogram of each compound in a vitamin drink and each spectrum
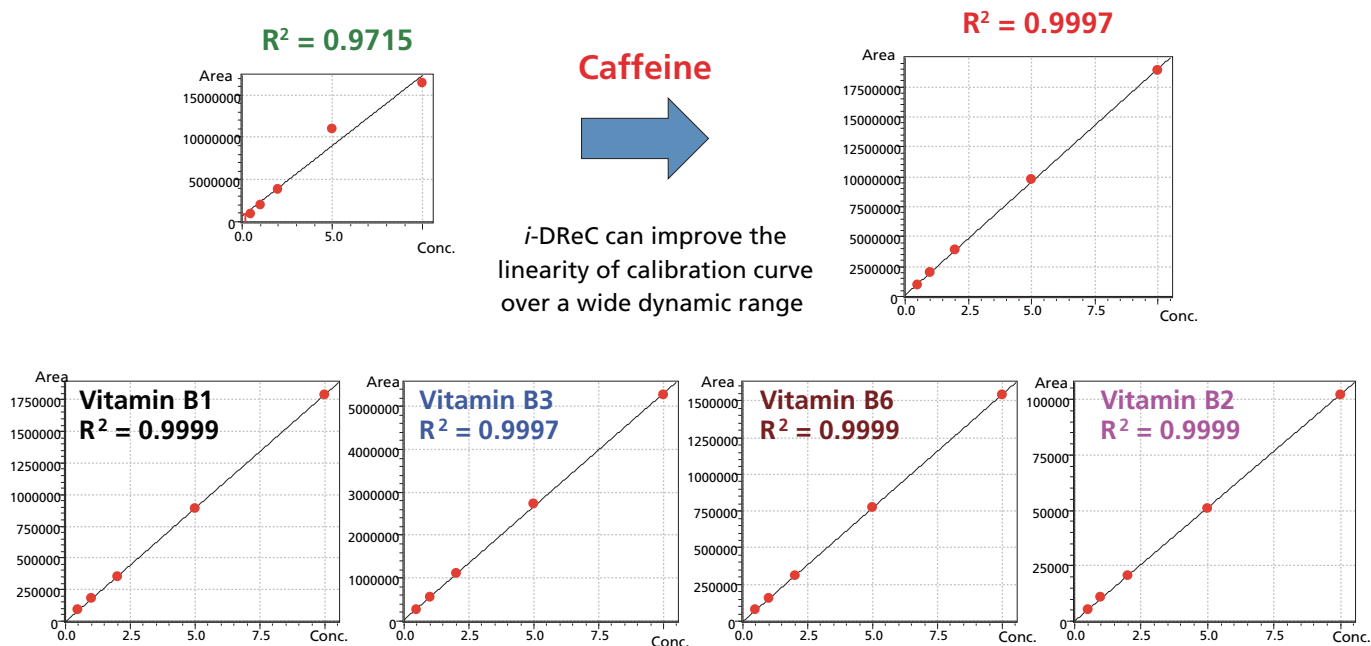

Figure 5: Calibration curve for each compound

Caffeine is the highest concentration among the ingredients. The results indicate that *i*-DReC can provide the wider dynamic range for the sample as higher concentration.

Conclusion

- The novel data processing method, *i*-DReC, can provide a wider dynamic range, more than 20 AU.
- *i*-DReC can save the labor effort for dilution for impurity analysis
- For simultaneous analysis of low and high concentration, *i*-DReC is also a powerful tool.

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