

# Analysis of Two Active Pharmaceutical Ingredients (API) Products Using UV Spectrophotometry with Multi-Component Analysis and a Fiber Optic Dissolution Analyzer

Andrew Kielt and Ishai Nir, Distek, Inc. - North Brunswick, New Jersey

## ABSTRACT

Traditionally, analyzing more than one active pharmaceutical ingredient (API) with UV spectrophotometry poses a challenge as both species often absorb over the same spectral region, causing deviations from Beer’s Law. This linear relation between absorbance and the absorbing species is used to calculate concentration values based on the measured absorbance at a specific wavelength. Separation techniques such as HPLC are often reverted to when analyzing mixture samples with more than one API due to the concentration calculation errors caused by the spectral overlap. However, Multicomponent Analysis (MCA) algorithm and complete spectral profiles collected using a fiber optic UV dissolution analyzer overcome these obstacles. This is accomplished using the Classical Least Squares form of Multiple Linear Regression to analyze the two spectrally overlapping components. The algorithm uses a calibration matrix of extinction coefficients derived from the spectra of multiple standard solutions to calculate component concentrations in an unknown mixture. This study demonstrates the MCA algorithm capability, used in tandem with in-situ fiber optics, to accurately monitor and quantify the dissolution profile of a commercial product containing two APIs, eliminating the need to draw samples for HPLC analysis.

## INTRODUCTION

This poster explains the theory behind the MCA algorithm methodology. Then, used in tandem with in-situ fiber optics, the accuracy of the technique is demonstrated by recovering the concentration of two APIs in known mixed solutions. Finally, an example is given of accurately monitoring and quantifying the dissolution profile of an actual commercial product containing two APIs, demonstrating the elimination of the need to draw samples or to perform HPLC analysis for many of these type of products.

In the case of dissolution, Classical Least Squares analysis involves the application of Multiple Linear Regression to the classical expression of the Beer’s law. Since complete UV spectra are measured, Beer’s law can be expanded to incorporate absorbance of multiple components at different wavelengths,  $\lambda$ :

$$A_{\lambda} = \sum_{j=1}^p E_{\lambda j} \cdot c_j$$

Where:

$A_{\lambda}$  = Absorbance of the mixture of p components at wavelength  $\lambda$

$E_{\lambda j}$  = Response sensitivity factor (molar absorptivity x probe path length) of component  $j$  at wavelength  $\lambda$

$C_j$  = Concentration of component  $j$  in the mixture

However, interactions between components including excipient materials also need to adequately represented. This leads to the need to expand the simple equation above into a more complex matrix:

$$A = K \cdot C$$

Where:

$A$  = Matrix of absorbance values for the calibration solutions

$K$  = Matrix of sensitivity factors determined from measured spectra of mixtures with known component concentrations.

$C$  = Matrix of known standard concentration values

$K$  is calculated using the concentration matrix  $C$ , its transpose  $C^T$ , and the calibration set absorbance matrix  $A_{std}$ .

$$K = A_{std} \cdot C^T \cdot [C \cdot C^T]^{-1}$$

From  $K$  and its transpose  $K^T$ ,  $K_{cal}$  (referred to as the calibration or regression matrix) can then be generated:

$$K_{cal} = [K^T \cdot K]^{-1} \cdot K^T$$

The least-squares solution to determining analyte concentrations in an unknown mixture is then determined by the applying  $K_{cal}$  to the measured absorbance values of the unknown mixture  $A_{unk}$ ,

$$C_{unk} = A_{unk} \cdot K_{cal}$$

$C_{unk}$  is the vector containing predicted concentration values ( $C_1, C_2, \dots, C_n$ ) for each analyte in the unknown mixture.

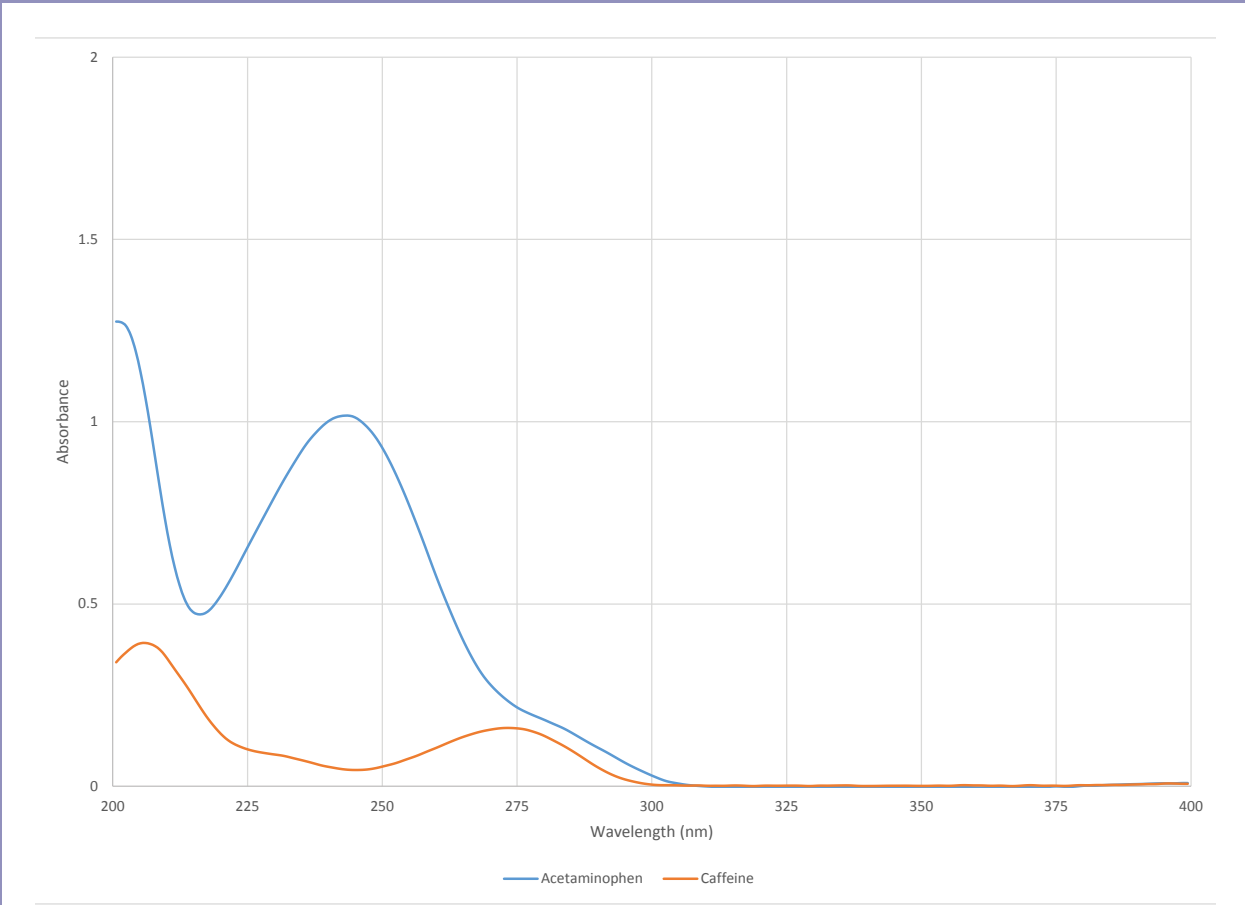


Figure 1. Absorbance spectra of Acetaminophen and Caffeine standards.



Figure 2. Comparison of measured versus actual results of standard mixtures.

Table 1. Measured versus actual percentage values of standard mixtures.						
Mixture %	Acetaminophen			Caffeine		
	Actual	% Measured	% Error	Actual	% Measured	% Error
1	50	50.43	0.9%	30	29.60	1.3%
2	30	30.30	1.0%	50	50.08	0.2%
3	90	89.83	0.2%	70	70.40	0.6%
4	70	70.19	0.3%	90	90.16	0.2%
5	100	99.68	0.3%	100	100.96	1.0%

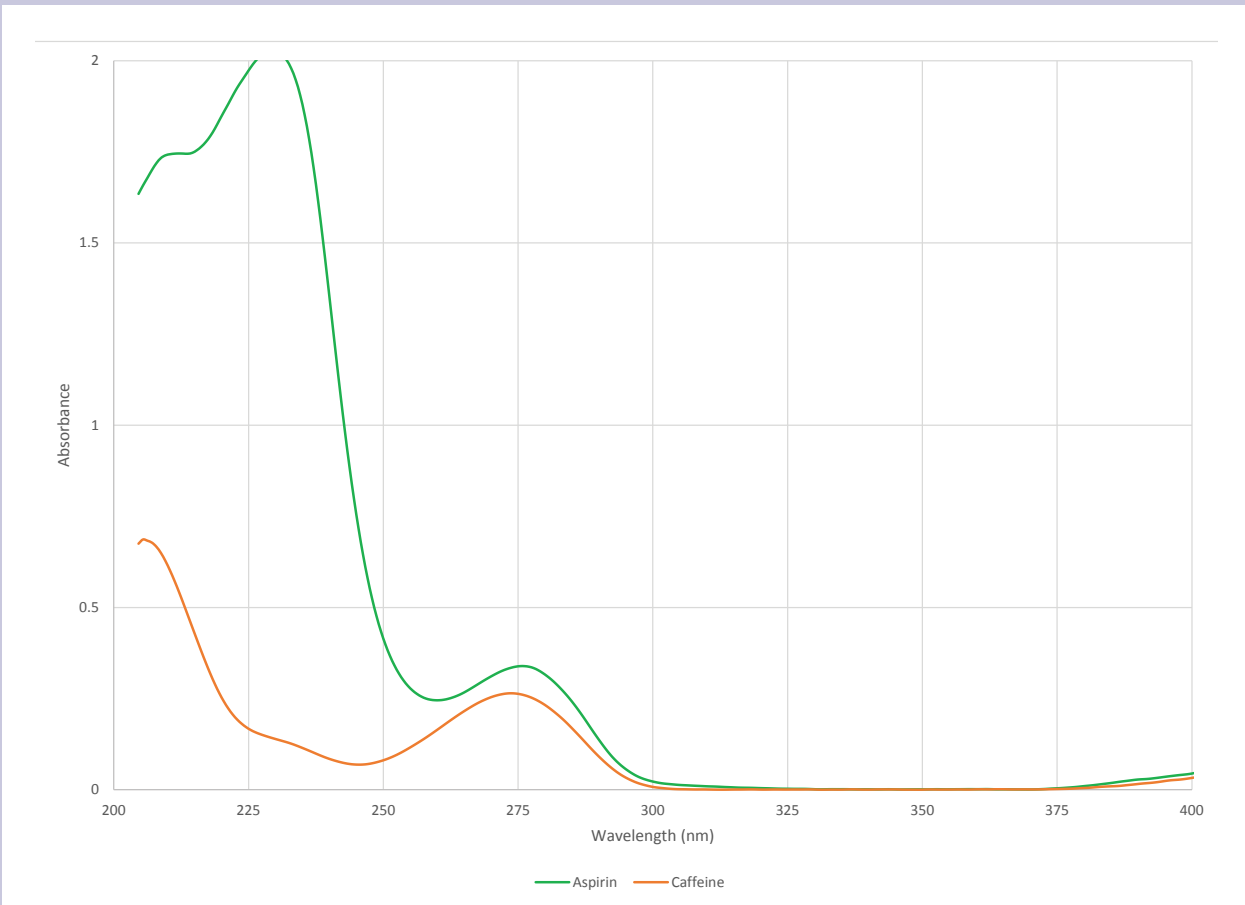


Figure 3. Absorbance spectra of Aspirin and Caffeine standards.

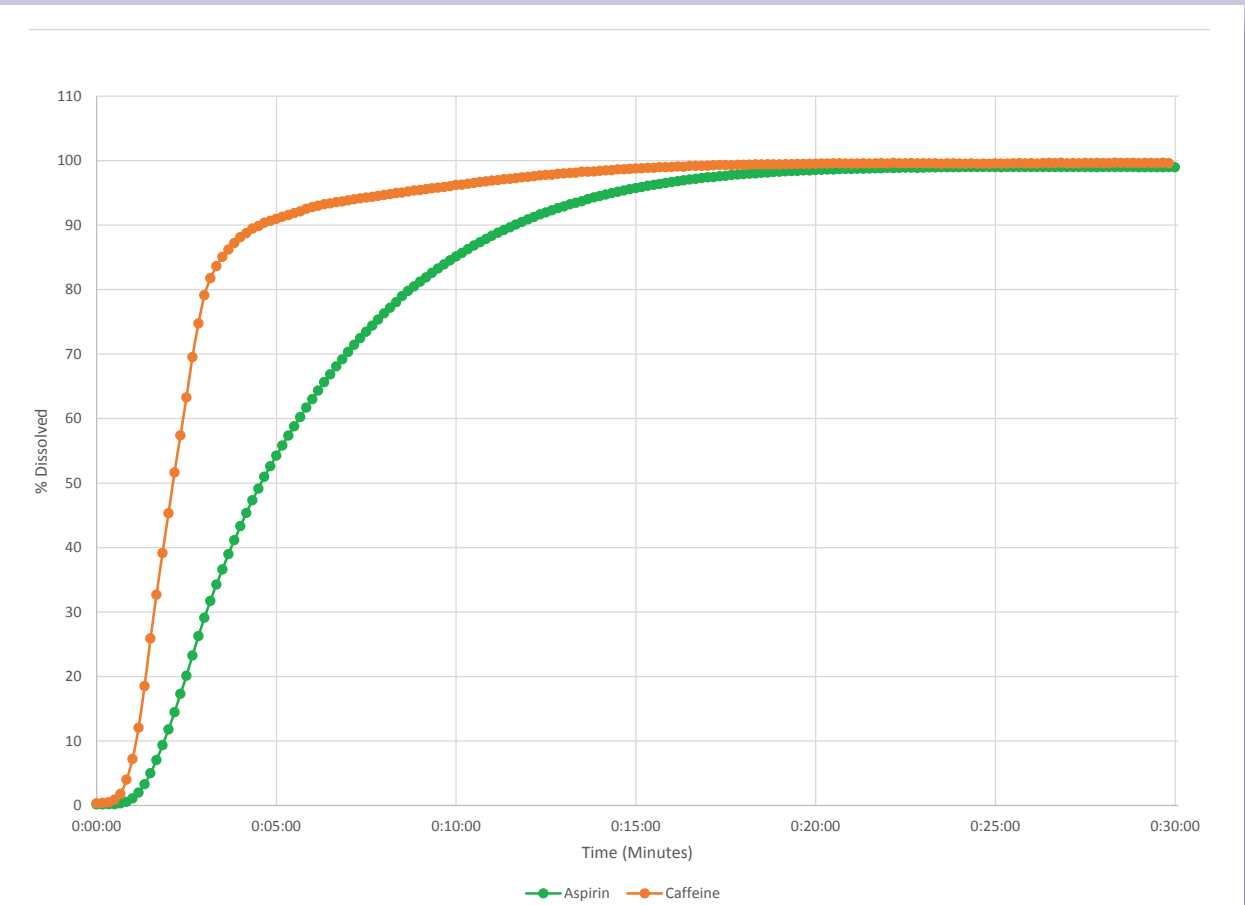


Figure 4. Average dissolution profile of six Aspirin Caffeine tablets.



## SUMMARY

UV spectrophotometry combined with MCA has been demonstrated to yield accurate analysis of the absolute concentrations of each component in two component mixtures. The technique has been also successfully applied to measuring the separate dissolution rates of two APIs in a commercially available product. These results demonstrate the method can accurately quantify two components even with highly overlapping spectra without the need for a separation step. The key to this process is using large data sets consisting of large spectral regions instead of individual wavelengths and complete temporal profiles instead of a few points. This rich data set collection is enabled by the use of in-situ sampling utilizing fiber optics probes which analyze the sample within the vessel. This circumvents the limit of the speed of moving the liquid from vessel to the analyzer that encumber traditional methods such as HPLC or conventional UV spectroscopy. An additional benefit of the instantaneous data collection of in-situ probes is that they allow near real-time dissolution analysis.

As these measurements of commercial products under real-world conditions illustrate, the addition of MCA and fiber optic in situ measurements allow formulation and analytical chemists, as well as QC analysts to realize the time and labor savings associate with UV spectrophotometry even when measuring products with two APIs.