APPLICATIONS

Ibuprofen Tablet USP Dissolution: A Rapid HPLC Alternative to the Traditional UV Method

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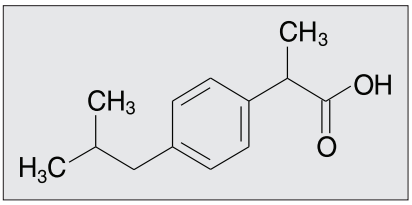
Introduction

Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) which is available in a variety of formulations, including tablets, capsules, chewables and oral suspension. In this tech note, we will demonstrate an alternative approach for the dissolution test for Ibuprofen tablets which utilizes the chromatographic assay method for Ibuprofen tablets instead of the UV method outlined in the USP monograph for dissolution testing. Two L1 columns with different dimensions within the allowable adjustments (USP General Chapter <621>) have been compared. With the use of an HPLC column for dissolution testing, the analysis time is less than 2 minutes and the peak is comparable with neat solution. Column loading capacity has been investigated in this study with different injection volumes.

Material

Ibuprofen



Ibuprofen standard was purchased from Sigma-Aldrich. The Ibuprofen 600 mg tablets were obtained from a local drug store.

Experimental Conditions

Dissolution Procedure

The dissolution sample was prepared based on the USP monograph for Ibuprofen tablets. 600 mg Ibuprofen tablets were dissolved in the pH 7.2 phosphate buffer medium. To prepare the dissolution medium, 6.89 g of sodium phosphate monobasic monohydrate (NaH_2PO_4 M.W. 137.99) was added to 800 mL of water, then adjusted to pH 7.2 with 50 % NaOH, and brought to 1000 mL in a volumetric flask.

Apparatus: basket, 50 RPM, 900 mL

Time points: a single time point was taken at 60 min

The sample was filtered through a Phenex™ 0.45 µm RC membrane syringe filter (P/N for Syringe filter: AF0-2103-52, and P/N for Disposable syringes plastic: AS0-8409)

Standard solution: 50 µg/mL in medium

Mobile Phase Preparation

The mobile phase was prepared per the USP assay method for Ibuprofen tablets by dissolving 4.0 g of chloroacetic acid into 400 mL water, adjusting to pH 3.0 with ammonium hydroxide, then mixing with 600 mL of acetonitrile.

LC-UV Conditions

Column: Kinetex® 5 µm C18
Dimensions: 150 x 4.6 mm
Part No.: 00F-4601-E0
Mobile Phase: 4.0 g Chloroacetic acid in water, pH 3.0 / Acetonitrile (40:60)
Flow Rate: 2.0 mL/min
Injection Volume 5 µL
Temperature: Ambient
Detection: UV @ 254 nm
Run Time: 4 minutes
Pressure: ~170 bar
System: Agilent® 1100 (Agilent Technologies®, Santa Clara, CA, USA)

LC-UV Conditions

Alternative column within allowable adjustment (L/dp between -25 % and +50 %, flow rate ± 50 %)

Column: Kinetex 2.6 µm C18
Dimensions: 75 x 4.6 mm
Part No.: 00C-4462-E0
Mobile Phase: 4.0 g Chloroacetic acid in water, pH 3.0 / Acetonitrile (40:60)
Flow Rate: 1.8 mL/min
Injection Volume 5 µL
Temperature: Ambient
Detection: UV @ 254 nm
Run Time: 4 minutes
Pressure: ~220 bar
System: Agilent® 1100 (Agilent Technologies®, Santa Clara, CA, USA)

Table 1.
USP tailing factor, peak height and efficiency with both columns used for the Ibuprofen dissolution sample

Kinetex C18, 5 µm, 150 x 4.6 mm			Kinetex C18, 2.6 µm, 75 x 4.6 mm		
Injection Volume (5 µL)					
USP Tailing factor	Peak Height	Efficiency (plates/meter)	USP Tailing factor	Peak Height	Efficiency (plates/meter)
1.122	12.11	89,607	0.963	18.94	121,107
Injection Volume (30 µL)					
1.252	65.94	79,093	1.261	100.75	103,840
Injection Volume (50 µL)					
1.395	106.29	74,007	1.242	159.4	93,880

Figure 1.
Representative chromatograms of neat solution vs. dissolution sample

Kinetex® C18 5 µm 150 x 4.6 mm, flow rate at 2.0 mL/min

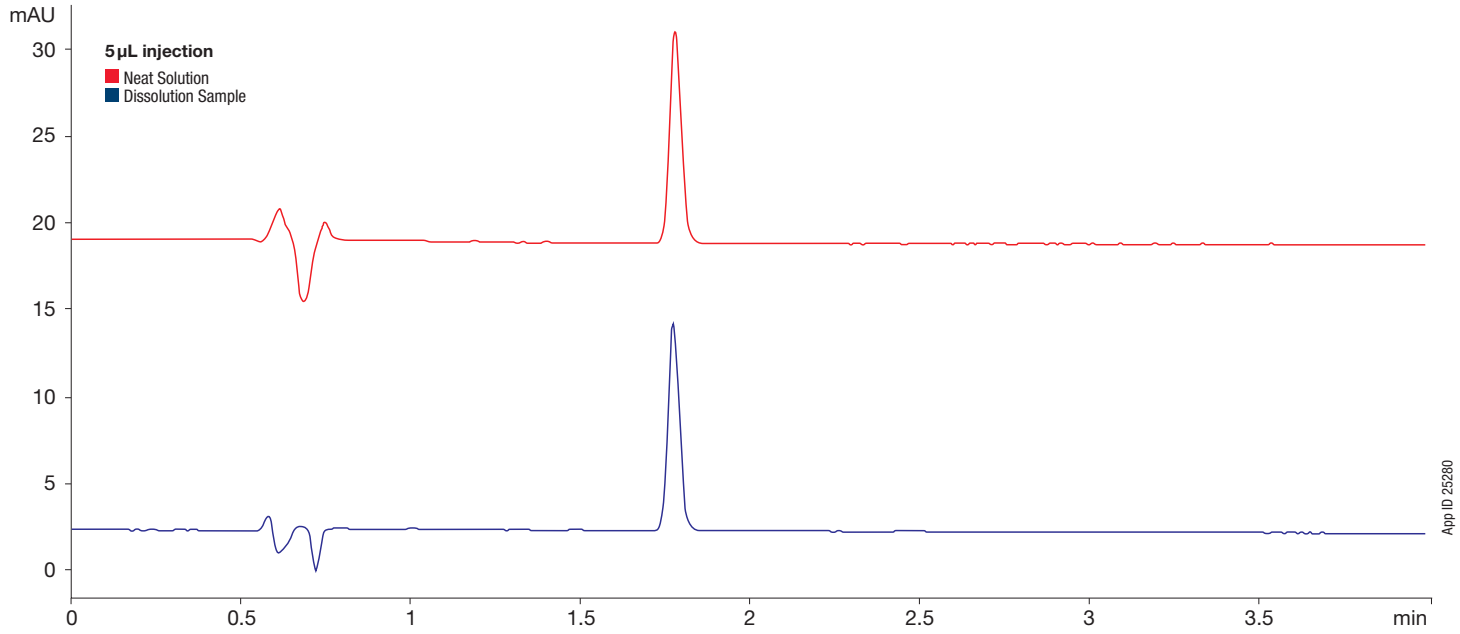


Figure 2.
Representative chromatograms of the column loading capacity test

Kinetex C18 5 µm 150 x 4.6 mm, flow rate at 2.0 mL/min

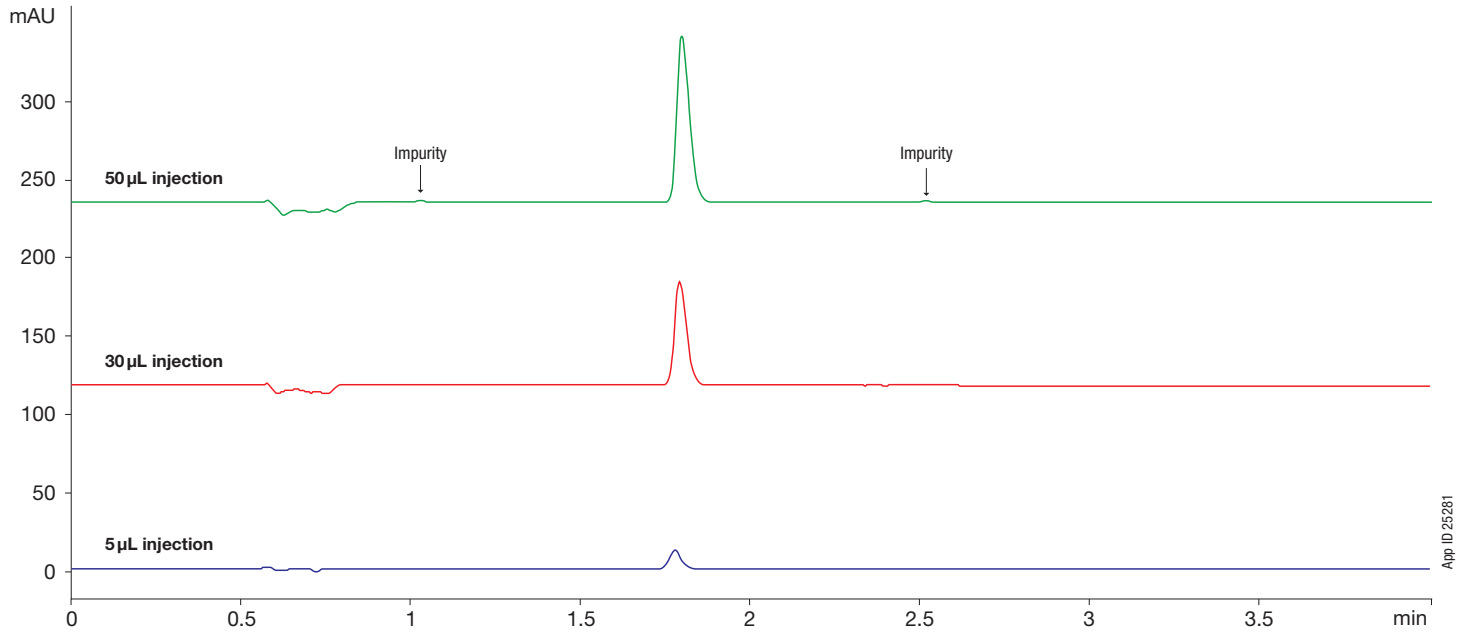


Figure 3.
Representative chromatograms of neat solution vs. dissolution sample

Kinetex® C18 2.6 µm 75 x 4.6 mm, flow rate at 1.8 mL/min

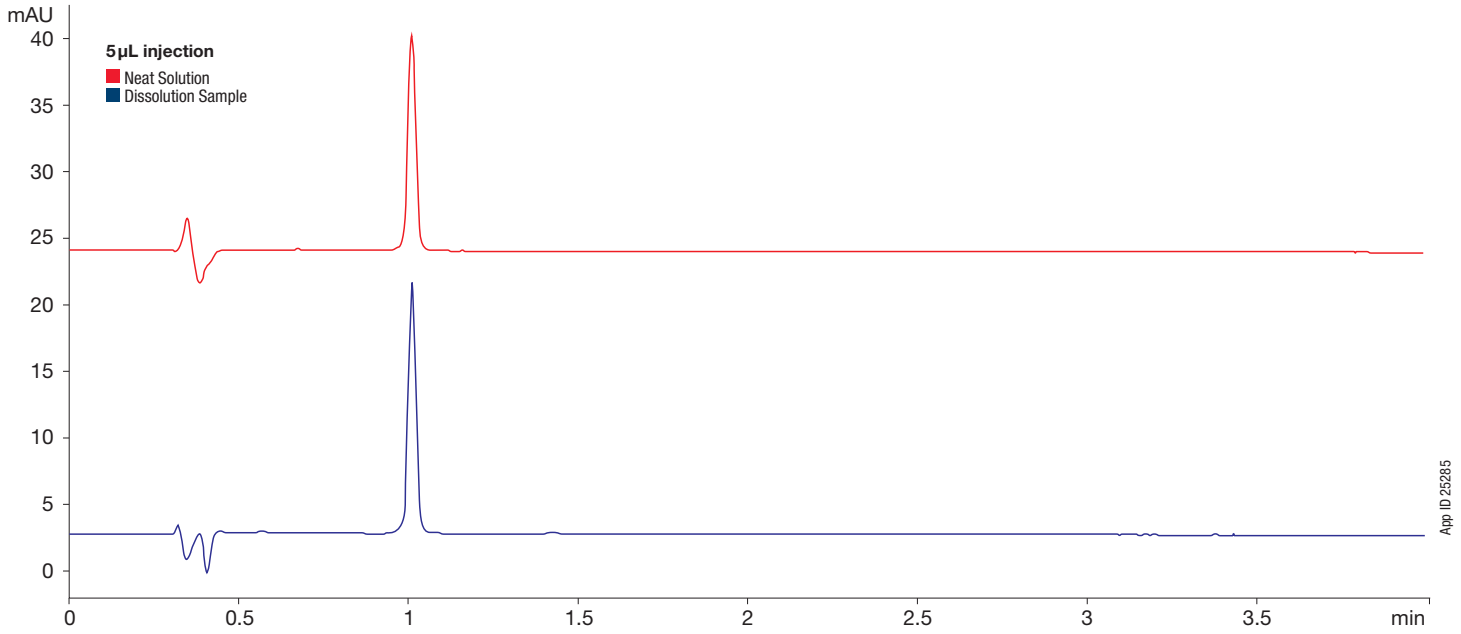
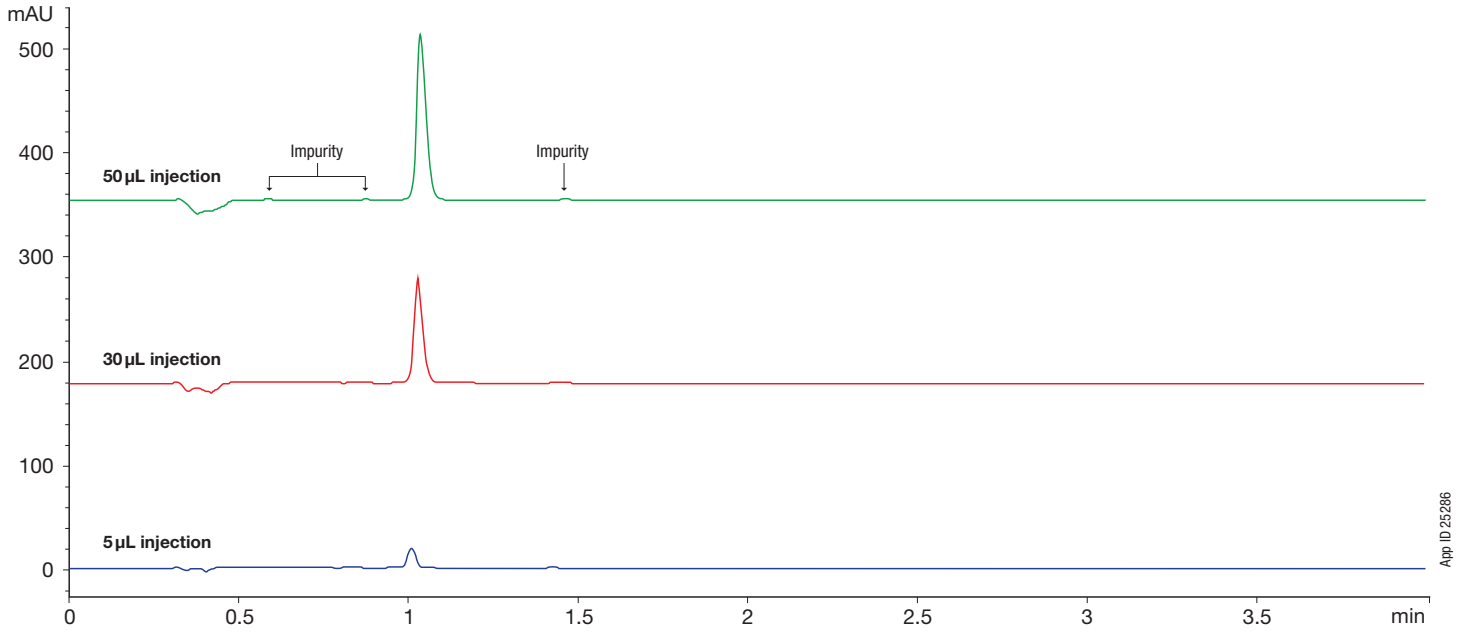


Figure 4.
Representative chromatograms of the column loading capacity test

Kinetex C18 2.6 µm 75 x 4.6 mm flow, rate at 1.8 mL/min



Results and Discussion

Figure 1 shows the chromatogram obtained for the Ibuprofen reference solution versus the dissolution sample injected on the Kinetex® C18 5 µm 150 x 4.6 mm column at a flow rate of 2.0 mL/min with a 5 µL injection volume. The retention time and peak shape of the dissolution sample is comparable with those of the reference solution. To be able to test column loading capacity, larger sample volumes were injected on to the Kinetex column (**Figure 2**). With the increasing injection volume, the peak height increased while the peaks associated with possible impurities also increased. However, adequate resolution between these impurity peaks and the Ibuprofen peak was maintained, thus using a larger injection volume would not compromise Ibuprofen quantitation in the dissolution solution.

Table 1 shows the USP tailing factor, peak height and efficiency obtained using the two Kinetex columns (different dimensions). As expected when mass loading is increased in HPLC, the tailing factor increased somewhat with the increase in injection volume - from 1.122 with a 5 µL injection volume to 1.395 with a 50 µL injection volume. The system suitability requirement for assay of Ibuprofen tablets is for the tailing factor to be no more than (NMT) 2.5, so the tailing factor observed for the dissolution sample easily meets this requirement. The signal intensity (peak height) is sufficient to allow for accurate quantitation of Ibuprofen in the dissolution sample. In some situations, for example a lower dosage form or extended release tablet or shorter dissolution time points, a larger injection volume might be required to obtain enough intensity for accurate quantitation. This examination of varying injection volumes, up to 50 µL illustrates that peak shape and intensity are still good.

USP General Chapter <621> allows for adjustments to the column dimension and particle size for isocratic methods. A smaller particle size or different column length can be utilized, as long as the ratio of column length (L) to particle diameter (dp) is maintained within -25% to +50% of the original column. The first column (Kinetex 5 µm C18 150 x 4.6 mm) has an L/dp ratio of 30,000; the second column used (Kinetex 2.6 µm C18 75 x 4.6 mm) has an L/dp ratio of 28,846, which is within the range of -25% to +50%, and is therefore an allowable adjustment to column dimension. The chromatograms obtained using the Kinetex 2.6 µm C18 75 x 4.6 mm column are shown in **Figures 3** and **4**. The samples were the same used with the original column (**Figures 1** and **2**). Since the use of the smaller particle size results in an increase in column back pressure, the flow rate was reduced to 1.8 mL/min to maintain the pressure within typical limits for HPLC systems. Per USP <621> the flow rate can be adjusted within the range of ± 50%. Even though this column (75 x 4.6 mm) is only half the length of the previous one (150 x 4.6 mm), the efficiency (plates/meter) is increased since a smaller particle size (2.6 µm) was used. This yields significant increase in peak intensity and narrower peak widths. The use of the shorter column reduces the analysis time, however, the backpressure of a 2.6 µm particle size column (~220 bar) will be much higher than a 5 µm column (~170 bar) even with the decrease in flow rate used here. If the back pressure is not a concern, the Kinetex 2.6 µm C18 75 x 4.6 mm would be an attractive option for reducing chromatographic analysis time. Here the retention time for Ibuprofen was reduced by about 50%.

Conclusion

In this adaptation of the USP dissolution method for Ibuprofen tablets, the amount of Ibuprofen dissolved has been determined by HPLC-UV comparing the UV absorbance of the sample solution with that of the standard solution. With the use of an HPLC analysis method for the dissolution sample, the observed peak intensity allowed for accurate quantitation of Ibuprofen in the dissolution sample to be achieved with an analysis time of less than 2 minutes. Two Kinetex columns with different dimensions within allowable adjustments were used to demonstrate this dissolution method. This dissolution assay was specifically adapted for the China bio-equivalence market to demonstrate an alternative approach utilizing chromatographic analysis to the traditional UV approach.

Ordering Information

Kinetex Core-Shell LC Columns

2.6 µm Analytical Columns (mm)						SecurityGuard ULTRA Cartridges‡
Phases	30 x 4.6	50 x 4.6	75 x 4.6	100 x 4.6	150 x 4.6	3/pk
C18	00A-4462-E0	00B-4462-E0	00C-4462-E0	00D-4462-E0	00F-4462-E0	AJ0-8768
						for 4.6 mm ID

5 µm Analytical Columns (mm)					SecurityGuard ULTRA Cartridges‡
Phases	50 x 4.6	75 x 4.6	100 x 4.6	150 x 4.6	3/pk
C18	00B-4601-E0	00D-4601-E0	00F-4601-E0	00G-4601-E0	AJ0-8768
					for 4.6 mm ID

‡SecurityGuard ULTRA Cartridges require holder, Part No.: AJ0-9000

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