Nota applicativa

Improved Chromatographic Analysis of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Using CORTECS™ Premier Columns That Feature MaxPeak™ High Performance Surfaces HPS Technology

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Abstract

NSAIDs are common pain-relieving anti-inflammatory medication used by millions of consumers worldwide, daily. To ensure the safety of consumers all around the globe, methods supporting the quality control sector of NSAIDs production are of great importance. In this application, we develop a rapid analysis for NSAIDs featuring CORTECS Premier Columns with MaxPeak HPS Technology. This method has proven to be reproducible and linear in its separation and detection of commonly used NSAIDs. Moreover, CORTECS Premier Columns that have MaxPeak HPS Technology showed improved chromatographic performance when compared to analysis on traditional CORTECS Columns packed in stainless-steel column hardware.

Benefits

- CORTECS Premier Columns with MaxPeak Technology improved chromatographic performance when compared to traditional stainless-steel systems and columns
- This method could analyze multiple NSAID compounds in under two minutes
- CORTECS Premier Columns with MaxPeak Technology delivers up to a 25% decrease in peak tailing and

39% increase to height signal when compared to traditional stainless-steel chromatographic systems

Introduction

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are common over the counter medicines used to relieve pain and reduce fevers.[1,2] Given the popularity and widespread use of NSAIDs, quality control testing for safety, and efficacy is of utmost importance. In this study, we provide a rapid method for the separation of NSAIDs. Further, we demonstrate the improvements CORTECS Premier Columns with MaxPeak HPS Technology has on NSAIDs analysis when compared to standard stainless-steel instruments, and columns.

NSAIDs are carboxylate containing analytes. It has previously been shown that metal surfaces in stainless-steel hardware interacts with carboxylate groups, which ultimately can cause poor chromatography.[3] These effects grow more apparent as stainless-steel systems corrode in the presence of highly acidic and/or chloride containing mobile phases. Recently, Waters Corporation introduced MaxPeak Premier Columns featuring new MaxPeak HPS Technology. The MaxPeak HPS Technology has been shown to mitigate some of these challenges, by preventing these undesirable metal and analyte interactions.[4,5,6]

Here, in this study we develop a rapid method to separate and quantitate common NSAIDs using CORTECS Premier Columns featuring MaxPeak HPS Technology. Also, we tested the lot consistency of CORTECS Premier Columns through comparing multiple injections of the same NSAIDs standard.

Experimental

Method of Separation Sample Description

Fenoprofen, diclofenac, naproxen, and ibuprofen were purchased from Sigma Aldrich (Milwaukee, WI). All NSAIDs were prepared as individual stocks at 1 mg/mL using 100% methanol as a diluent. Then, fenoprofen, diclofenac, and naproxen stock standards were diluted and combined at a 50 µg/mL concentration in the NSAIDs mix standard. Ibuprofen was combined into the NSAIDs mix at 500 µg/mL given the analyte's low UV absorbance at 270 nm. Stock solutions were stored at 2 °C–8 °C and allowed to equilibrate to ambient room

temperature prior to analysis.

Linearity Sample Description

The diclofenac curve stock standard was prepared at a 1 mg/mL concentration and diluted using 100% methanol into a 10 mL volumetric flask. Then, various calibration standards were prepared from the stock ranging from 5 µg/mL to 500 µg/mL. Stock solutions were stored at 2 °C–8 °C and allowed to equilibrate to ambient room temperature prior to analysis.

Method Conditions

Two instrument set-ups were used in this study; an ACQUITY Premier LC System set up to showcase the MaxPeak HPS Technology and a traditional stainless-steel ACQUITY UPLC I-Class LC. Each system was ran using the same instrument conditions, just different components.

LC Conditions

System set-up	Premier MaxPeak HPS	Traditional stainless-steel
LC system:	ACQUITY™ Premier LC System	ACQUITY UPLC™ I-Class System
Detection:	Waters™ Arc™ Premier 2998 Photodiode Array Detector, 270 nm	Waters™ 2998 Photodiode Array Detector, 270 nm
Column(s):	CORTECS™ Premier C_{18} 2.1 × 50 mm, 1.6 µm	CORTECS™ C_{18} 2.1 × 50 mm, 1.6 µm
Column temp.:	30° C	
Sample temp.:	Ambient	
Injection volume:	0.5 µL	
Flow rate:	0.8 mL/min	
Mobile phase A:	0.1% Formic acid in DI water	
Mobile phase B:	0.1% Formic acid in acetonitrile	

Gradient Table

Time (min)	Flow (mL/min)	%A	%B	Curve
Initial	0.8	65	35	6
2.40	0.8	50	50	6
2.50	0.8	20	80	6
2.60	0.8	20	80	6
2.61	0.8	65	35	6
3.00	0.8	65	35	6

Data Management

Chromatography software: The Empower 3 Software Build 3471

Results and Discussion

Method of Separation Results

This method was found to be reproducible in the retention and separation of common NSAIDs. After ten injections, the %RSD for area and retention time for all NSAIDs were ≤5% (Table 1 and Table 2). Below, an overlay chromatogram of the ten injections provides a clear picture of the method's performance (Figure 1a).

Area reproducibility	Naproxen (µV*sec)	Fenoprofen (µV*sec)	Diclofenac (µV*sec)	Ibuprofen (µV*sec)
Mean	40781	11047	58340	17524
Std. dev	388	95	512	173
%RSD	0.95	0.86	0.88	0.99

Table 1. Table containing the %RSDs for the area counts from the NSAIDs mix standard.

Retention time reproducibility	Naproxen (min)	Fenoprofen (min)	Diclofenac (min)	Ibuprofen (min)
Mean	0.79	1.28	1.62	1.72
Std. dev	0.00	0.00	0.00	0.00
%RSD	0.18	0.12	0.09	0.09

Table 2. Table containing the %RSDs for the retention times from the NSAIDs mix standard.

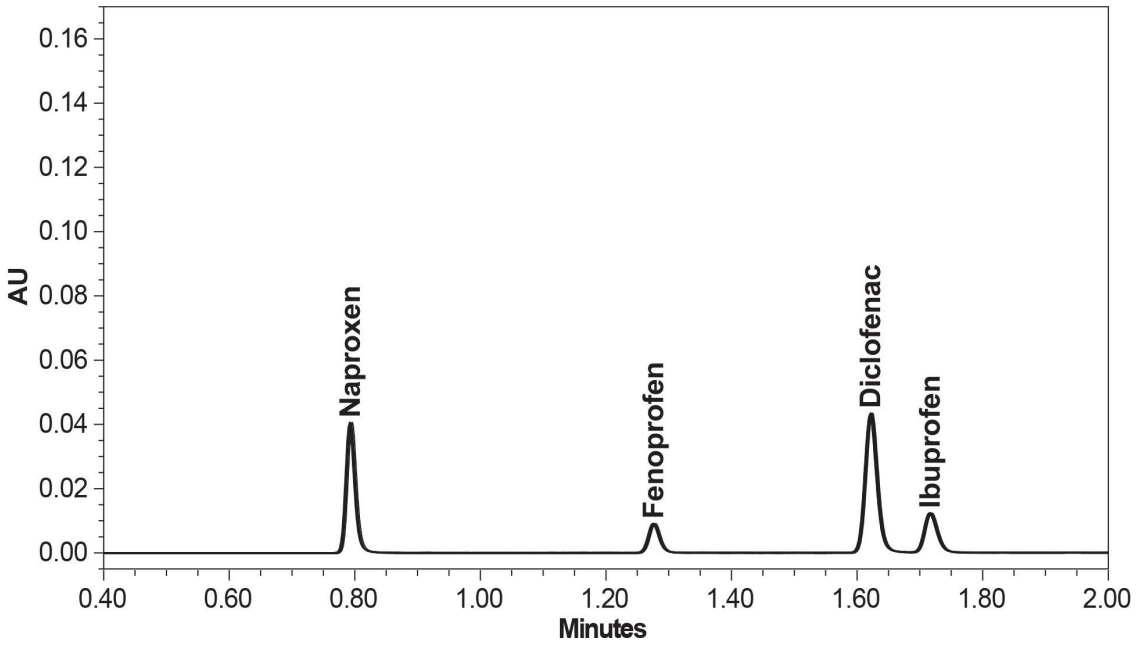


Figure 1a. An overlay chromatogram of ten injections of the NSAIDs mix standard.

Linearity Results

Linearity was performed on diclofenac to demonstrate the quantitative suitability for this method. The linear data collected supports its use for quality control testing (Figure 2).

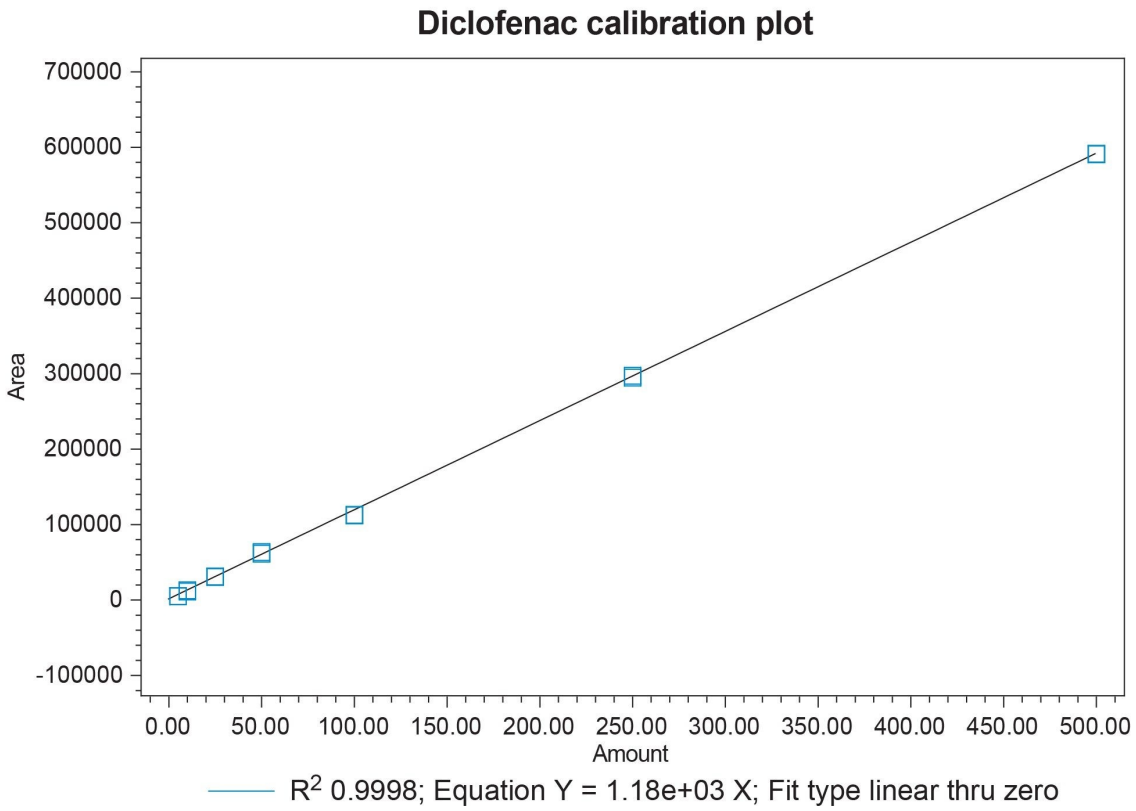


Figure 2. Seven-point calibration curve for diclofenac spanning from 5 µg/mL to 500 µg/mL. The R^2 value for the curve was ≥0.999.

System Comparison Results

This method was transferred onto a stainless-steel system to highlight the improvements of CORTECS Premier Columns with MaxPeak HPS Technology has on NSAIDs analysis. Ten injections of the NSAIDs mix standard were injected onto each of the instrument configurations. In figures 3a and 3b below, both systems were shown to run the method successfully.

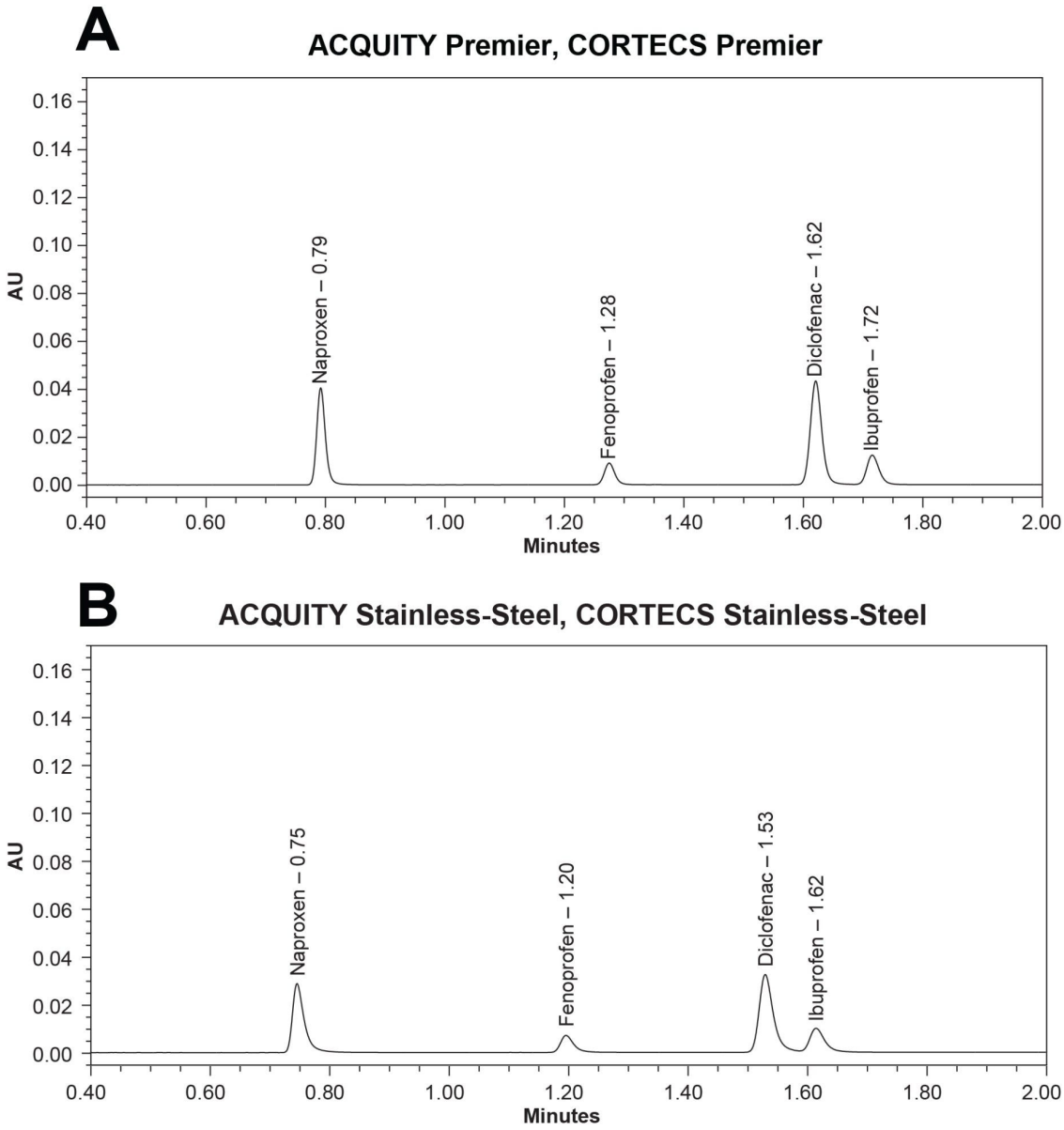


Figure 3a. Chromatogram for injection five out of ten of the NSAIDs mix standard on the ACQUITY Premier System equipped with a CORTECS Premier C_{18} Column.

Figure 3b. Chromatogram for injection five out of ten of the NSAIDs mix standard on the ACQUITY I-Class System equipped with a CORTECS C_{18} Column.

The chromatographic data for figures 3a and 3b is detailed in tables 3 and 4, respectively. Here, a clear picture of

the benefits of CORTECS Premier Columns with MaxPeak HPS Technology is shown. This technology offers up to a 25% decrease in tailing and 39% increase in height.

NSAID name	Retention time (min)	Area (AU)	Height	USP resolution (half-height)	USP tailing
Naproxen	0.79	40819	40462		1.18
Fenoprofen	1.28	11071	9032	16.81	1.14
Diclofenac	1.62	58435	43286	10.42	1.14
Ibuprofen	1.72	17607	12287	2.64	1.19

Table 3. Chromatographic data for figure 3a.

NSAID name	Retention time (min)	Area (AU)	Height	USP resolution (half-height)	USP tailing
Naproxen	0.75	39647	28913		1.58
Fenoprofen	1.20	10823	7100	12.56	1.37
Diclofenac	1.53	52644	32500	8.42	1.30
Ibuprofen	1.62	15932	9585	2.02	1.44

Table 4. Chromatographic data for figure 3b.

Lot to Lot Reproducibility Results

To demonstrate the batch repeatability of the new Premier line of columns three injections of the NSAIDs mix standard were performed. Each column was installed on the Premier System set-up, allowed to equilibrate, and injected with the standard. Three column lots were compared below (Figure 4 and Table 5).

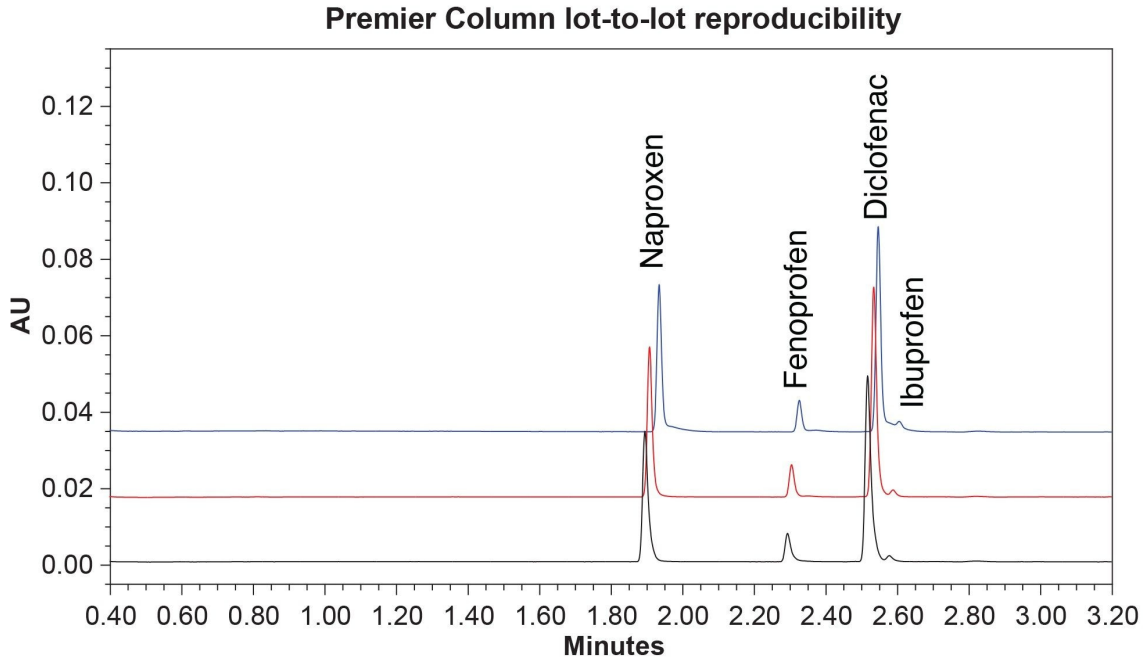


Figure 4. Overlay chromatogram of the NSAIDs Mix for three different column lots; Lot A (Black), Lot B (Red), and Lot C (Blue).

	Average retention time for the NSAID over 3 injections			
Column lot	**Naproxen**	**Fenoprofen**	**Diclofenac**	**Ibuprofen**
A	1.90	2.30	2.52	2.58
B	1.91	2.31	2.54	2.59
C	1.94	2.33	2.55	2.61
%RSD between lots	1.09	0.75	0.59	0.57

Table 5. The calculated averages over the course of three injections for the retention time of analytes across all the column lots.

The overlay chromatogram, and %RSDs for retention time suggests that the CORTECS Premier Columns reliably perform across different sorbent batches. This provides confidence to consumers who choose CORTECS Premier

Columns.

Conclusion

Here, the use of CORTECS Premier Columns with MaxPeak HPS technology improved the analysis of NSAIDs when compared to a traditional stainless-steel chromatography set up. The method produced is efficient and gives results in two minutes. CORTECS Premier Columns provided significant improvements in peak shape and performed consistently across different sorbent batches.

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720007751, January 2023

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