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Application Note

Advantages of Using MaxPeak™ HPS Technology for the Analysis of Non-Steroidal Anti-Inflammatory Drugs

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This is an Application Brief and does not contain a detailed Experimental section.

Abstract

Pharmaceutical laboratories are routinely tasked with developing fast, sensitive, and robust methods to monitor manufacturing, formulation, and stability of chemical entities. The physiochemical properties of pharmaceutical compounds upon injection on chromatographic systems can result in sample loss, variability, or asymmetrical peak shapes. In such cases, it is important to develop a dependable chromatographic analytical method to minimize surface interactions.

In this application, NSAIDs were utilized as candidate molecules to show the benefits of employing MaxPeak HPS technology. NSAIDs were selected for this demonstration because of their behavior as free radical scavengers. This reactivity exhibits a propensity towards analyte complexation with metal ions when exposed to alloy derived componentry present in chromatographic systems and columns. This complexation leads to low chromatographic recovery when strong ion-pairing additives or long system passivation sequences are not employed. MaxPeak HPS technology overcomes these challenges to promote an improved chromatographic

response, without the need for mobile phase additives or passivation.

Benefits

- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) exhibit greater peak height and area response when using MaxPeak High Performance Surfaces (HPS) technology compared to analysis with conventional chromatographic systems and columns
- MaxPeak HPS technology exhibits improved chromatographic sensitivity when analyzing NSAIDs without the need for strong mobile phase additives, chelators, or lengthy passivation protocols

Introduction

NSAIDs are some of the most commonly used pharmaceuticals. Apart from analgesic, anti-inflammatory, and antipyretic efficacies, these compounds offer protection against diverse critical disorders including cancer and heart attacks. NSAIDs have structural and functional diversity, but most are weak organic acids comprised of an acidic moiety (carboxylic acid, enol) and an aromatic functional group (Figure 1).[1]

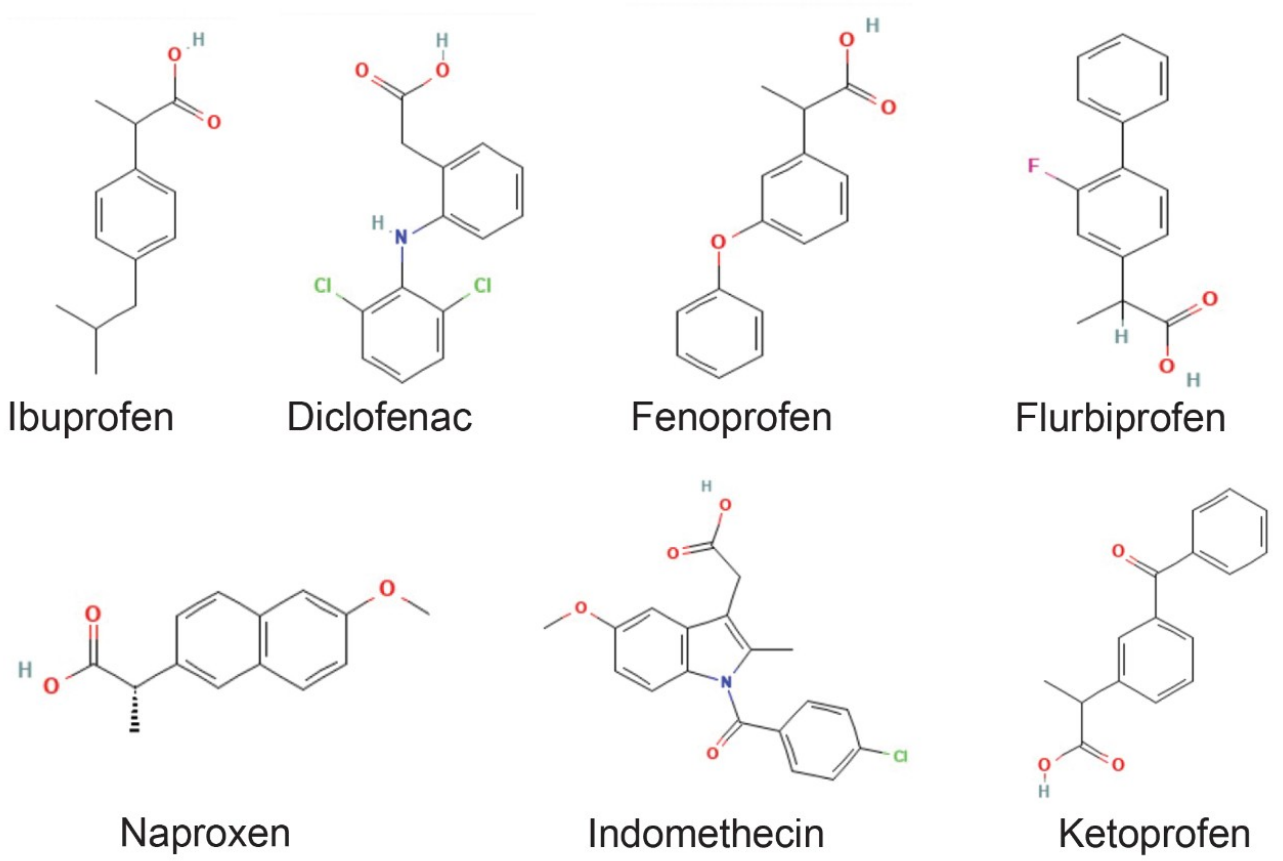

Figure 1. Structures of the propionic acid and acetic acid derivative NSAIDs used in this study.[4]

Although a high propensity for reactivity is the primary mechanism thought to contribute to NSAID anti-inflammatory effects, these free radical scavengers can be a challenge to analyze accurately. When exposed to system and column surfaces comprised metal alloys, formation of NSAID/non-specific metal-ion complexes may significantly reduce chromatographic sensitivity. Mobile phase ion-pairing agents and chelating agents, such as 0.1% trifluoracetic acid (TFA), are sometimes added to improve chromatographic peak shape, but use of these reagents can result in system contamination, irreversible alterations in column selectivity, high background interference, and low sensitivity in both ultraviolet (UV) and liquid chromatography-mass spectrometry (LC-MS) applications.[2,3]

MaxPeak HPS technology is designed to provide exceptional chromatographic performance, by minimizing analyte/surface interactions for metal-ion sensitive, free radical scavenging compounds. The objective of the work shown here is to compare the chromatographic performance of MaxPeak HPS technology with a

conventional chromatographic system when analyzing NSAIDs that are propionic acid and acetic acid derivatives.

Experimental

Materials and Methods

LC system 1:	ACQUITY™ Arc™ System with Quaternary Solvent Manager (rQSM), Sample Manager (rFTN), ACQUITY Arc Column Manager (rCM), Empower™ 3 Chromatography Software
LC system 2:	Arc Premier System with Quaternary Solvent Manager (rQSM), Arc Premier Sample Manager (rFTN), Empower 3 Chromatography Software
Detection:	ACQUITY Array Detector (PDA) with detection at 215 nm for ibuprofen and ketoprofen, all other compounds observed at 265 nm
Column(s):	XBridge™ XP, BEH™ C_{18}, 2.5 µm Column, 4.6 x 150 mm, p/n: 186006711 XBridge Premier, BEH C_{18}, 2.5 µm Column, 4.6 x 150 mm, p/n: 186009849
Column temp.:	50 °C
Sample temp.:	20 °C
Injection volume:	0.5 µL

Flow rate:	1.3 mL/min
Diluent:	(50/50) Methanol/water
Mobile phase A:	10 mM Ammonium formate pH 4.0
Mobile phase B:	Acetonitrile
Conditions:	(50/50) Mobile phase A/Mobile phase B, Isocratic

Results and Discussion

Individual NSAID stock solutions of ibuprofen, ketoprofen, fenoprofen, naproxen, diclofenac, flurbiprofen, and indomethacin (Sigma-Aldrich, St. Louis, MO) were prepared in sample diluent at approximately 0.4 mg/mL. To avoid influences from potential passivation by mobile phase new columns were employed. Systems were flushed thoroughly with 100% isopropyl alcohol followed by HPLC grade water. The same UV detector was utilized for each system setup to ensure continuity. For data analysis, the UV response recorded in the Empower 3 Software when using MaxPeak HPS technology was compared to the response obtained with the conventional system and column setup.

Chromatographic peak height and area sensitivity increased for all NSAIDs when MaxPeak HPS technology was utilized (Figure 2, Figure 3, Table 1, Table 2). With the XBridge Premier Column, the height response increased up to 1.6-fold (38%), and the area response increased up to 1.7-fold (41%). When the Arc Premier System was paired with a XBridge Premier Column, an even greater increase in height response of up to 4.7-fold (79%) was observed, while the area response increased up to 4.0-fold (75%).

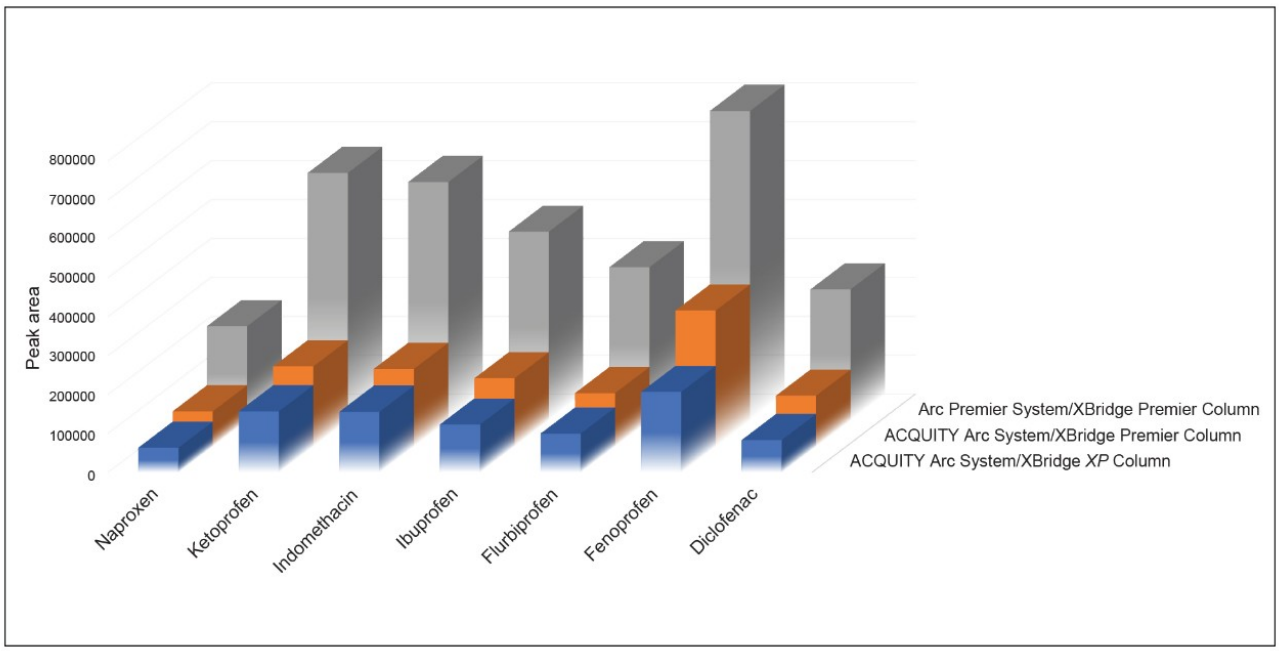

Figure 2. Increase in chromatographic peak area with MaxPeak HPS technology.

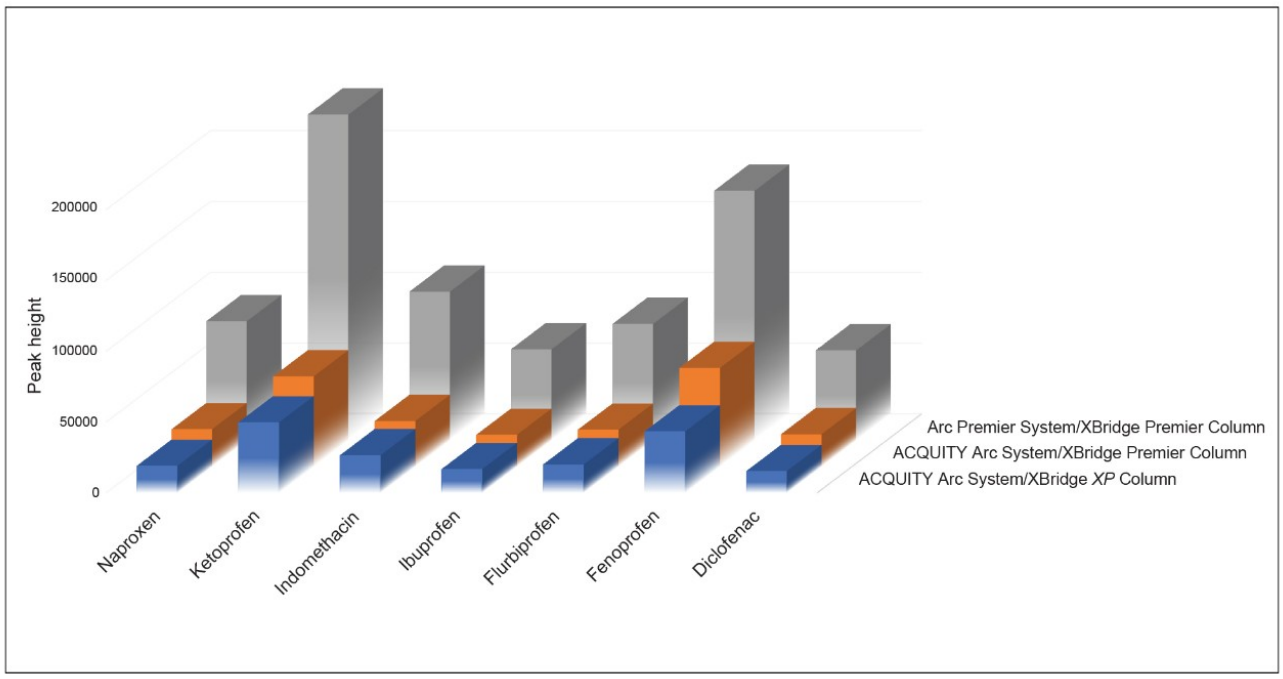

Figure 3. Increase in chromatographic peak height with MaxPeak HPS technology.

NSAID	Fold increase in height with the XBridge Premier Column	Fold increase in height with the ACQUITY Arc Premier System/ XBridge Premier Column
Naproxen	1.4	4.4
Ketoprofen	1.3	4.7
Indomethacin	1.2	4.0
Ibuprofen	1.3	3.8
Flurbiprofen	1.3	4.1
Fenoprofen	1.6	4.1
Diclofenac	1.5	4.1

Table 1. Fold increase in peak height with the MaxPeak HPS technology compared to the conventional ACQUITY Arc System/XBridge XP Column.

NSAID	Fold increase in area with the XBridge Premier Column	Fold increase in area with the ACQUITY Arc Premier System/ XBridge Premier Column
Naproxen	1.4	3.8
Ketoprofen	1.3	4.0
Indomethacin	1.3	3.9
Ibuprofen	1.4	3.9
Flurbiprofen	1.4	3.9
Fenoprofen	1.7	3.8
Diclofenac	1.6	4.0

Table 2. Fold increase in peak area with MaxPeak HPS technology compared to the conventional ACQUITY Arc System/XBridge XP Column.

Conclusion

NSAIDs, are pharmaceutically active compounds with analgesic, antipyretic, and anti-inflammatory effects. MaxPeak HPS technology was shown to promote significantly greater peak height and area response during chromatographic analysis of NSAID compounds. Further, the improved sensitivity provided by the MaxPeak HPS technology would correspond to obtaining increased detection limits for NSAID compounds when compared to analysis with a conventional chromatographic system and column.

References

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