

Chiral HPLC of NSAIDs (Profens) Utility of Chirex™ Chiral Stationary Phases

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Introduction

NSAIDs, or non-steroidal anti-inflammatory drugs, belong to a class of compounds called profens. They are characterized by an asymmetric carbon center attached to a carboxylic acid, a methyl, and an aryl group of varying structure. Clinical activity centers on the ability of these compounds to inhibit prostaglandin synthesis. NSAIDs represent one of the most commercially successful and important classes of analgesic anti-inflammatory drugs. Examples include, Ibuprofen, which is one of the most widely-used over-the-counter pain relievers, and Naproxen, one of the most successful prescription drugs in this class ever marketed.

Generally, profens are given in racemic form (both enantiomers are present, and have analgesic properties). In vivo, however, some profens can undergo, to a limited degree, inversion from the R to the S form. This leads to an enantiomeric excess of the S form, which has been an area of concern and investigation.¹

Although the patient has the metabolic burden of two distinct chemical entities (the R and S enantiomers) when a NSAID is given as a racemate, there is currently no compelling evidence to suggest that the R enantiomer poses any significant toxicological hazard.

The primary reason for the continued use of racemic NSAIDs today is probably economic. However, in view of both regulatory and economic pressures for single S or R enantiomer formulations (termed "racemic switching") of chiral NSAIDs – to improve the therapeutics and to extend patent life – it may not be long before single enantiomer administration is the rule, rather than the exception for this important class of drugs.

In this Technical Note, simple and direct chiral HPLC methods for the resolution of racemic NSAIDs (profens) are described.²

Instrumentation & Equipment

Analyses were performed using an HP 1100 LC system (Agilent Technologies, Palo Alto, CA, USA) equipped with a quaternary pump, in-line degasser, multi-wavelength detector, and autosampler. HP Chemstation software was used for the data analysis. The HPLC columns used for the analysis are Chirex™ brand (Phenomenex, Torrance, CA, USA, see Ordering Information). Standards were purchased from Sigma (St. Louis, MO), Aldrich (Milwaukee, WI), or Fluka (Ronkonkoma, NY), depending on availability.

Results & Discussion

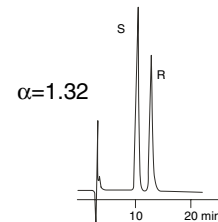
In the Applications below various Chirex™ chiral stationary phases (CSPs) were evaluated for their utility to directly resolve (without derivatization) enantiomers of some important NSAIDs Profen drugs.

Table 1. Enantioresolution of NSAIDs-Profen Drugs using Chirex CSPs

NSAID	Chirex Phase	Alpha Factor	App ID No.
2-Phenylpropionic acid	3005	1.05	13932
Fenoprofen	3005	1.10	13923
Flurbiprofen	3005	1.09	13925
Ibuprofen	3005	1.05	13928
Indoprofen	3005	1.08	13939
Ketoprofen	3005	1.15	5245
Naproxen	3005	1.32	13944
Pranoprofen	3005	1.13	5244

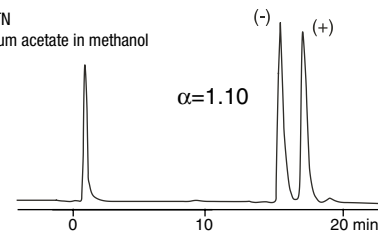
App ID 13944 Naproxen

Column: Chirex 3005
Dimensions: 250 x 4.0mm
Order No.: 00G-3005-D0-TN
Mobile Phase: 0.03M Ammonium acetate in methanol
Flow Rate: 0.8mL/min
Conditions: UV @ 254nm



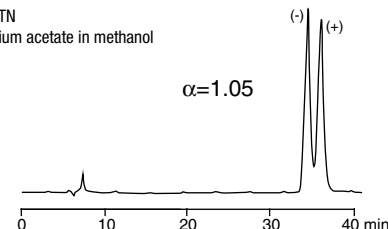
App ID 13923 Fenoprofen

Column: Chirex 3005
Dimensions: 250 x 4.6mm
Order No.: 00G-3005-E0-TN
Mobile Phase: 0.02M Ammonium acetate in methanol
Flow Rate: 0.8mL/min
Conditions: UV @ 254nm



App ID 13928 Ibuprofen

Column: Chirex 3005
Dimensions: 250 x 4.6mm
Order No.: 00G-3005-E0-TN
Mobile Phase: 0.01M Ammonium acetate in methanol
Flow Rate: 0.5mL/min
Conditions: UV @ 254nm



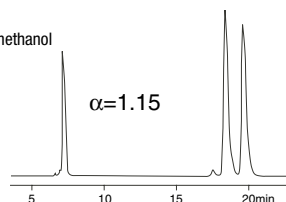
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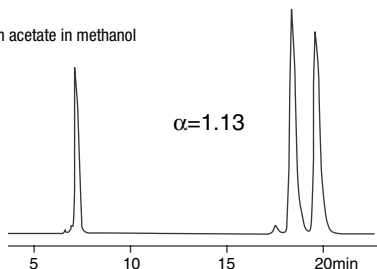
App ID 5245 Ketoprofen

Column: Chirex 3005
Dimensions: 250 x 4.0mm
Order No.: 00G-3005-D0-TN
Mobile Phase: 0.03M Ammonium acetate in methanol
Flow Rate: 1.0mL/min
Conditions: UV @ 254nm



App ID 5244 Pranoprofen

Column: Chirex 3005
Dimensions: 250 x 4.6mm
Order No.: 00G-3005-E0-TN
Mobile Phase: 0.02M Ammonium acetate in methanol
Flow Rate: 0.8mL/min
Conditions: UV @ 254nm



Ordering Information:

Chirex is available in a wide range of phases and column sizes, from analytical to preparative. All phases are also available in bulk (15 and 30μ particle size).

The columns discussed in this Note are listed below.

5μ Analytical Columns (mm)

Chirex Phase and Bond Linkage, 250 x 4.6mm ID

Phase	Description	Order No.
3005	(R)-NGLY and DNB Covalent Amide	00G-3005-E0-TN

CHIREX™

References

1. Brown, J.M. *Science*, 257, 1847, **1992**.
2. Cleveland, T., J. Liq. Chromatogr. 18(4): 649-671, **1995**.

If you would like more information on these chiral columns or any of the applications listed, please contact Phenomenex. Also, if you are new to chiral HPLC or are doing method development work call us today to reserve your **FREE** copy of our 70-page **Guidebook to Chiral HPLC Method Development**.

