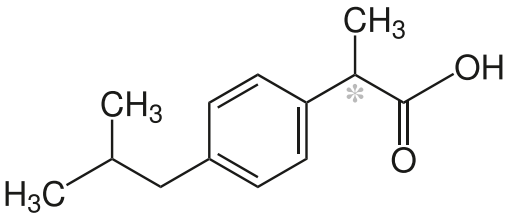

Ibuprofen and Valerophenone – USP

MACHEREY NAGEL application department · Dr. H. R. Wollseifen, T. Kretschmer, R. Nuessgen

Application benefits

- HPLC method with faster separations within allowable adjustments.
- Shorter runtimes
- Lower solvent consumption
- Optimized system suitability

MN products

REF 760103.46
EC HPLC column (analytical), NUCLEODUR® C18 Gravity, 5 µm, 150 × 4.6 mm

REF 763156.46
EC HPLC column (analytical), NUCLEOSHELL® RP 18, 5 µm, 150 × 4.6 mm

REF 763134.20
EC HPLC column (analytical), NUCLEOSHELL® RP 18, 2.7 µm, 100 × 2 mm

REF 702107
Screw closure, N 9, PP, yellow, center hole, Silicone white/PTFE red, 1.0 mm

REF 702079
Screw neck vial, N 9, 11.6 × 32.0 mm, 1.5 mL, label, flat bottom, amber, silanized

MN application numbers

HPLC: 129420
HPLC: 129430
HPLC: 129440

Keywords

Ibuprofen, Valerophenone, USP, NUCLEOSHELL® RP18, NUCLEODUR® C18 Gravity, L1, United States Pharmacopeia

Introduction

The USP monograph describes the separation of Ibuprofen and Valerophenone. This work starts using a fully porous HPLC phase and shows the benefits using superficially porous particles. The method optimization was performed to achieve shorter run times and system suitability results within allowable adjustments.

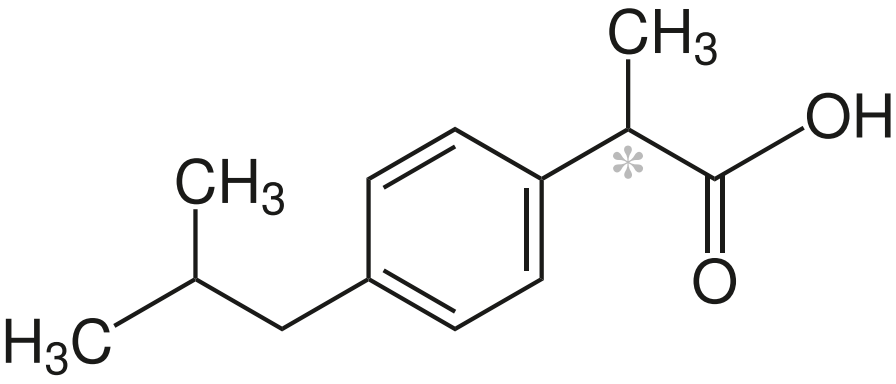

Figure 1: Structure of Ibuprofen.

USP Monograph: Ibuprofen Method Details

Method Parameter	Description
Resolution solution	Prepare a solution in acetonitrile containing in each mL about 5 mg of Ibuprofen* and 5 mg of Valerophenone.
Column size	150 × 4.0 mm
Stationary phase	5-µm packing L1
Mobile phase	Prepare a suitable filtered mixture of water, previously adjusted with phosphoric acid to pH 2.5 and acetonitrile (1340:680).
Flow rate	2.0 mL/min
Temperature	30 °C
Detection	214 nm
Injection	5 µL
Elution order	1. Valerophenone 2. Ibuprofen
Suitability requirements Resolution:	NLT 2.0 between Valerophenone and Ibupofen.

* Ibuprofen (USP-1335508 was purchased from Labmix24 GmbH; Postal address: Industriestrasse 18A - 46499 Hamminkeln (Germany).

Table 1: USP Monograph: Ibuprofen Method Details

Chromatographic methodology improvements

Figure 2: a

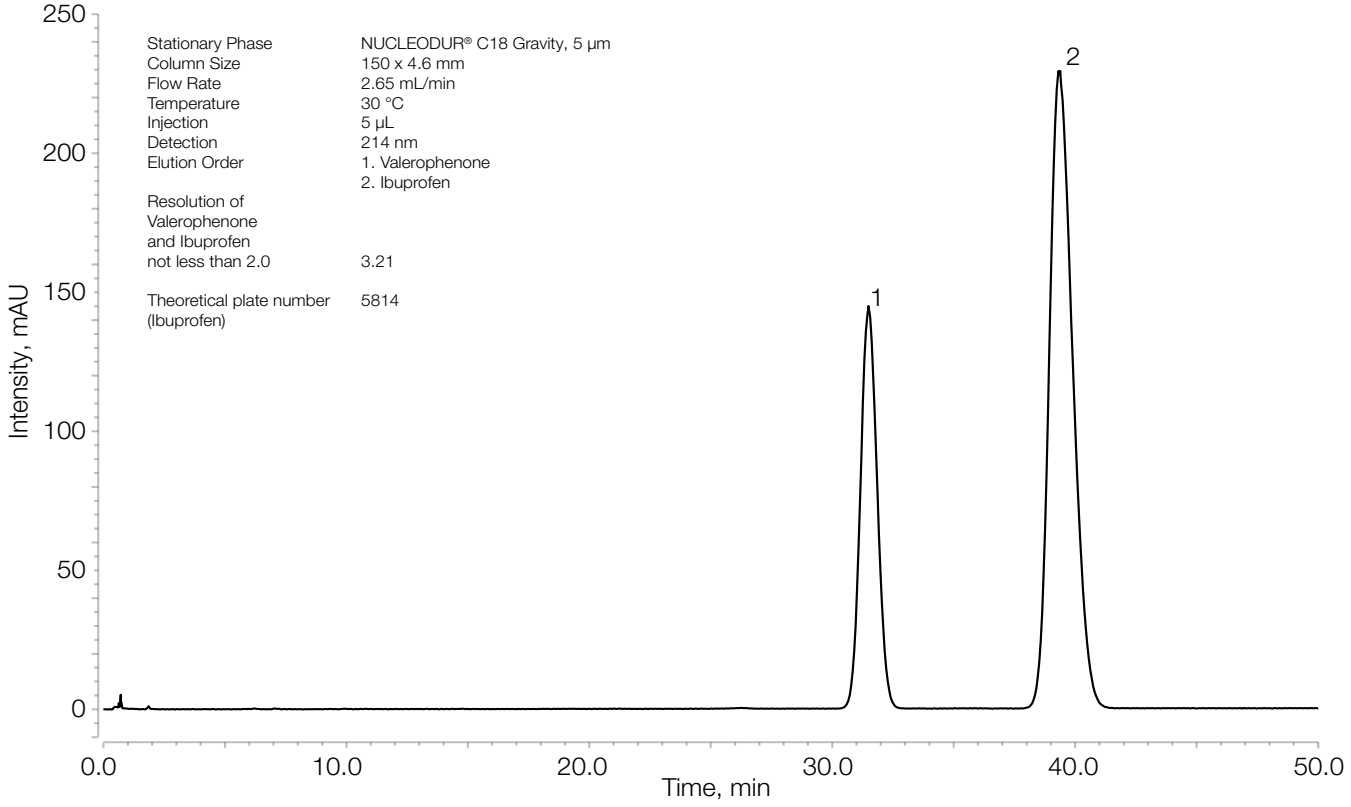

Figure 2: b

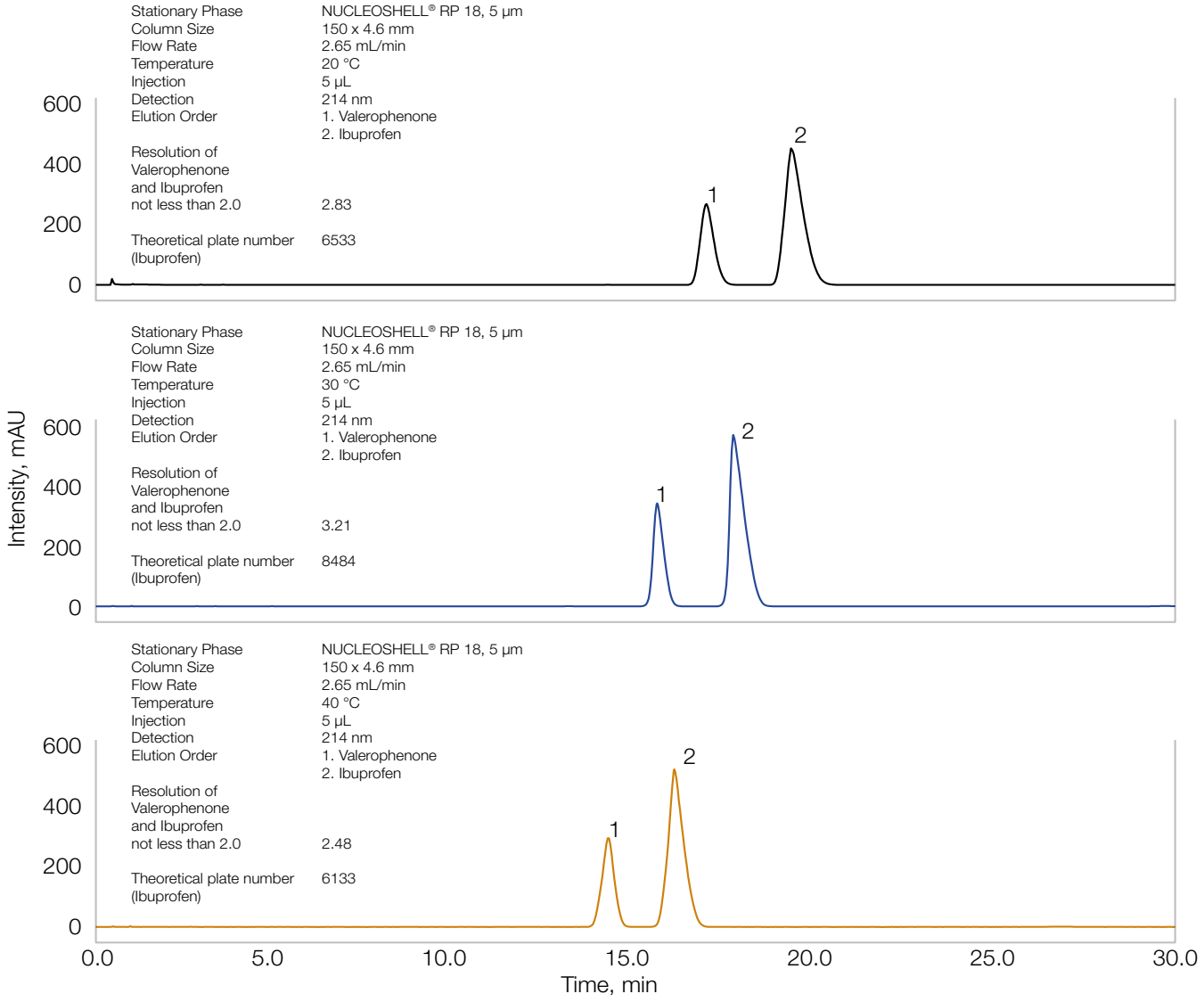
Stationary Phase NUCLEOSHELL® RP 18, 5 µm
Column Size 150 x 4.6 mm
Flow Rate 2.65 mL/min
Temperature 20 °C
Injection 5 µL
Detection 214 nm
Elution Order 1. Valerophenone 2. Ibuprofen
Resolution of Valerophenone and Ibuprofen not less than 2.0 2.83
Theoretical plate number (Ibuprofen) 6533
Stationary Phase NUCLEOSHELL® RP 18, 5 µm
Column Size 150 x 4.6 mm
Flow Rate 2.65 mL/min
Temperature 30 °C
Injection 5 µL
Detection 214 nm
Elution Order 1. Valerophenone 2. Ibuprofen
Resolution of Valerophenone and Ibuprofen not less than 2.0 3.21
Theoretical plate number (Ibuprofen) 8484
Stationary Phase NUCLEOSHELL® RP 18, 5 µm
Column Size 150 x 4.6 mm
Flow Rate 2.65 mL/min
Temperature 40 °C
Injection 5 µL
Detection 214 nm
Elution Order 1. Valerophenone 2. Ibuprofen
Resolution of Valerophenone and Ibuprofen not less than 2.0 2.48
Theoretical plate number (Ibuprofen) 6133
Intensity, mAU
600
400
200
0
1
2
0.0
5.0
10.0
15.0
20.0
25.0
30.0
Time, min

Figure 2: c

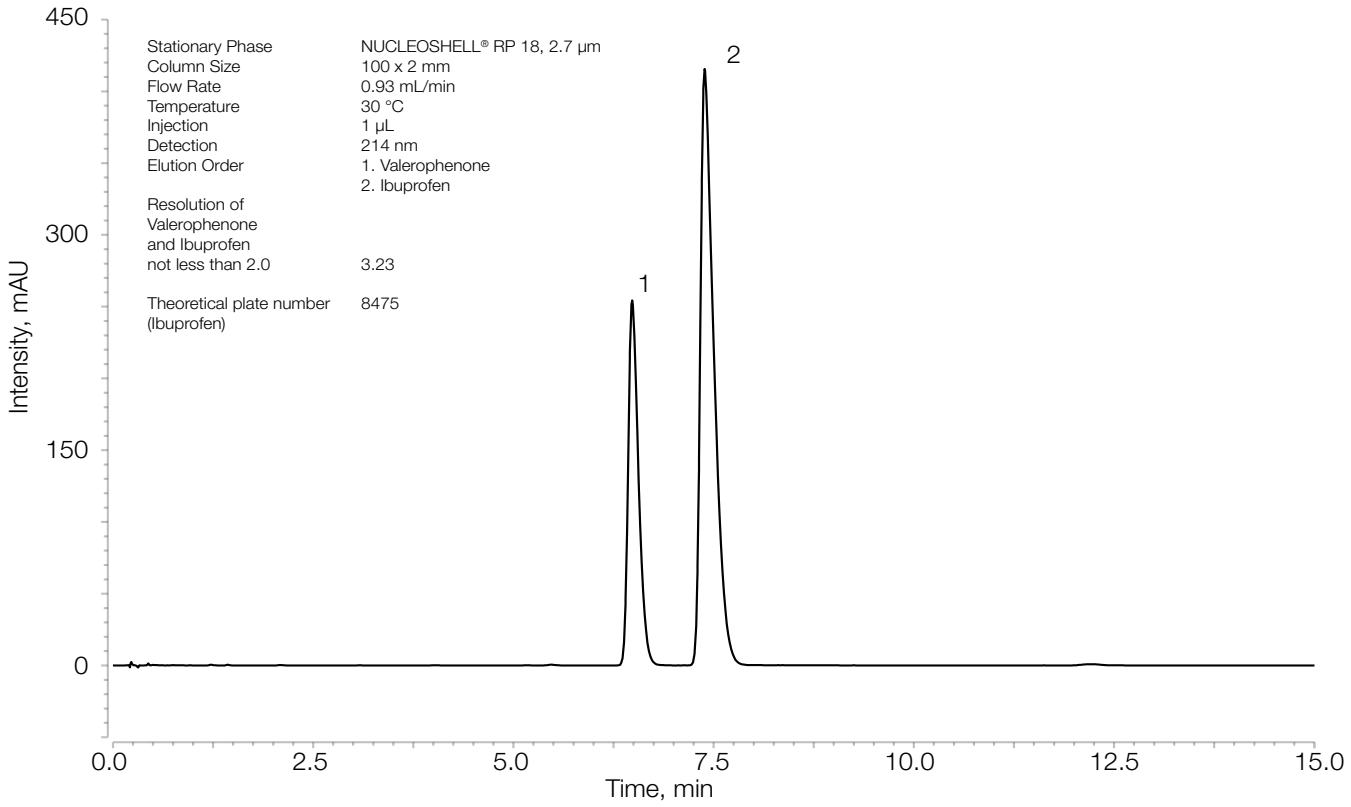

Figure 2: a: EC HPLC column (analytical), NUCLEODUR® C18 Gravity, 5 µm, 150 × 4.6 mm; b: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 5 µm, 150 × 4.6 mm, Temperature: top: 20 °C, middle: 30°C, bottom: 40 °C; c: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 2.7 µm, 100 × 2 mm.

Results

Method Parameter	Allowed Adjustments (isocratic elution)	Method 1 (figure 2: a)	Method 2 (figure 2: b)	Method 3 (figure 2: c)
Mobile phase pH	± 0.2 units	As specified	As specified	As specified
Concentration of salts in buffer	± 10%	As specified	As specified	As specified
Composition of the mobile phase	± 30% relative; cannot exceed ± 10% absolute change; cannot be reduced to zero	As specified	As specified	As specified
Stationary phase	No change of C18 allowed	NUCLEODUR® C18 Gravity	NUCLEOSHELL® RP 18	NUCLEOSHELL® RP 18
Ratio column length/particle size	Column length to particle size diameter ratio can be adjusted between -25% and +50%	150 mm / 5 µm as specified	150 mm / 5 µm as specified	100 mm / 2.7 µm (+ 23%*)
Column internal diameter	Can be adjusted so long as linear velocity is maintained	4.6 mm as specified	4.6 mm as specified	2 mm
Flow rate	± 50% after adjustment due to a change in column dimensions	2.65 mL/min (± 0% after adjustments)	2.65 mL/min (± 0% after adjustments)	0.93 mL/min (± 0% after adjustments)
Column temperature	± 10 °C	30 °C as specified	20 °C 30 °C as specified 40 °C	30 °C as specified
Injection volume	Can be adjusted as much as needed; must be consistent with linearity, precision, and detection requirements	5 µL as specified	5 µL as specified	1 µL
Detection [nm]	No change permitted	214 nm as specified	214 nm as specified	214 nm as specified
Retention time Ibuprofen [min]		39.432 min	19.388 min (– 50.8%**) 17.736 min (– 55.0%**) 16.051 min (– 59.3%**)	7.380 min (– 81.3%**)
Theoretical plate number (Ibuprofen)	Within –25% to 50%, relative to the prescribed column***	5814	6533 (+ 12.4%**) 8484 (+ 45.9%**) 6133 (+ 5.5%**)	8475 (+ 45.8%**)
Suitability requirements				
Resolution:	NLT 2.0 between Valerophenone and Ibuprofen.	4.62	2.83 3.21 2.48	3.23

* change in comparison to USP method ** change in compatison to method 1 *** column used in method 1

Conclusion

The fully porous NUCLEODUR® C18 Gravity, 5 µm, 150 × 4.6 mm HPLC column from MACHEREY NAGEL fulfills all requirements of the USP monograph (Ibuprofen and Valerophenone). By using superficially porous NUCLEOSHELL® analytical columns the runtime of the method can be reduced by up to 81.3 % (with NUCLEOSHELL® RP 18, 2.7 µm, 100 × 2 mm) compared to fully porous NUCLEODUR® silica gel, while keeping all method parameters well within the allowed adjustment range of the USP monograph. The reduction in runtime leads to a lower solvent consumption optimizing the analysis of Ibuprofen with regard to the guidelines of green chemistry. We were also able to improve the peak intensity with NUCLEOSHELL® columns compared to the original method with fully porous silica gel.

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MACHEREY-NAGEL GmbH & Co. KG · Valencienner Str. 11 · 52355 Düren · Germany
DE +49 24 21 969-0 info@mn-net.com
CH +41 62 388 55 00 sales-ch@mn-net.com
FR +33 388 68 22 68 sales-fr@mn-net.com
US +1 888 321 62 24 sales-us@mn-net.com