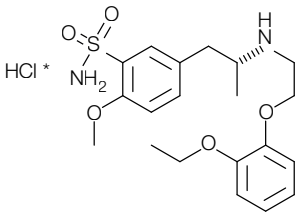


Tamsulosin Hydrochloride and Related Substances – Ph. Eur. monograph 2131

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 763156.46
EC HPLC column (analytical), NUCLEOSHELL® RP 18, 5 µm, 150x4.6 mm

REF 763134.46
EC HPLC column (analytical), NUCLEOSHELL® RP 18, 2.7 µm, 100x4.6 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, 11.6x32.0 mm, 1.5 mL, label, flat bottom, amber, silanized

MN application numbers

HPLC: 129450 HPLC: 129460

Keywords

Tamsulosin Hydrochloride, Ph. Eur. monograph 2131, NUCLEOSHELL® RP 18, L1, European Pharmacopeia

Introduction

The Ph. Eur. Monograph 2131 describes the separation of Tamsulosin Hydrochloride from impurities. This seperation can be achieved by using a superficially porous HPLC phase. Further method optimization leads to shorter run times and lower solvent consumption while keeping the system suitability parameters well within the allowed adjustment ranges.

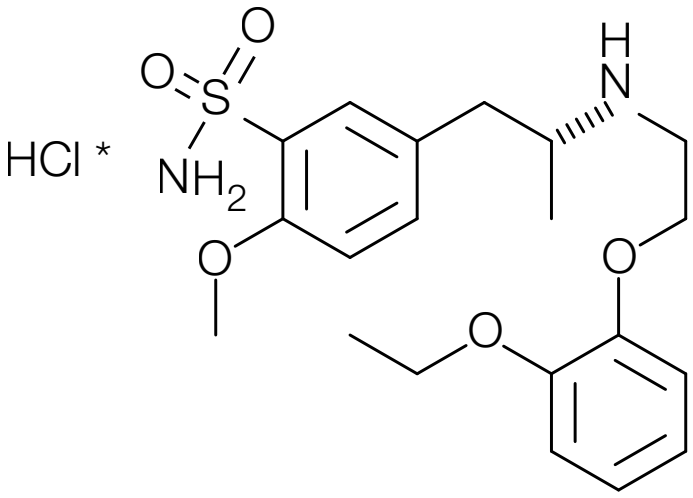


Figure 1: Tamsulosin

Ph. Eur. Monograph 2131 method parameters (a)

Method Parameter	Description
Reference Solution	(b) Dissolve 4 mg of Tamsulosin Impurity D CRS* and 4 mg Tamsulosin Hydrochloride CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 20.0 mL with the mobile phase.
Column Size	150 x 4.6 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Dissolve 3.0 g of sodium hydroxide R in a mixture of 8.7 mL of perchloric acid R and 1.9 L of water R; adjust to pH 2.0 with 0.5 M sodium hydroxide and dilute to 2 L with water R; to 1.4 L of this solution, add 600 mL of acetonitrile R.
Flow Rate	1.3 mL/min
Temperature	40 °C
Detection	UV, 225 nm
Injection	10 µL
Run Time	1.5 times the retention time of Tamsulosin
Elution Order	1. Impurity D 2. Tamsulosin
System Suitability Requirements Resolution (Reference Solution b):	NMT 6.0 between Impurity D and Tamsulosin

* Tamsulosin impurity D CRS* (Y0000651), Tamsulosin Impurity H CRS (Y0000652) and Tamsulosin Hydrochloride CRS (Y0000650) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Table 1a: Ph. Eur. Monograph 2131 Details Method (a).

Ph. Eur. Monograph 2131 method parameters (b)

Method Parameter	Description
Reference Solution	(c) Dissolve 4 mg of Tamsulosin Impurity H CRS*, 4 mg of Tamsulosin Impurity D CRS* and 4 mg Tamsulosin Hydrochloride CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase. Dilute 2.0 mL of this solution to 20.0 mL with the mobile phase.
Column size	150 x 4.6 mm
Stationary Phase	End-capped octadecylsilyl silica gel for chromatography R (5 µm)
Mobile Phase	Dissolve 3.0 g of sodium hydroxide R in a mixture of 8.7 mL of perchloric acid R and 1.9 L of water R; adjust to pH 2.0 with 0.5 M sodium hydroxide and dilute to 2 L with water R; add 2 L of acetonitrile R.
Flow Rate	1.0 mL/min
Temperature	40 °C
Detection	UV, 225 nm
Injection	10 µL
Run Time	5 times the retention time of Tamsulosin
Elution Order	1. Impurity D 2. Tamsulosin 3. Impurity H
System Suitability Requirements Resolution (Reference Solution c):	NMT 2.0 between Tamsulosin and Impurity H

* Tamsulosin impurity D CRS* (Y0000651), Tamsulosin Impurity H CRS (Y0000652) and Tamsulosin Hydrochloride CRS (Y0000650) were purchased from European Directorate for the Quality of Medicines & HealthCare (EDQM) – Council of Europe; Postal address: 7 Allee Kastner CS 30026F - 67081 STRASBOURG (France).

Table 1b: Ph. Eur. Monograph 2131 Details Method (b).

Chromatographic methodology improvements for (a) and (b)

Figure 2: a

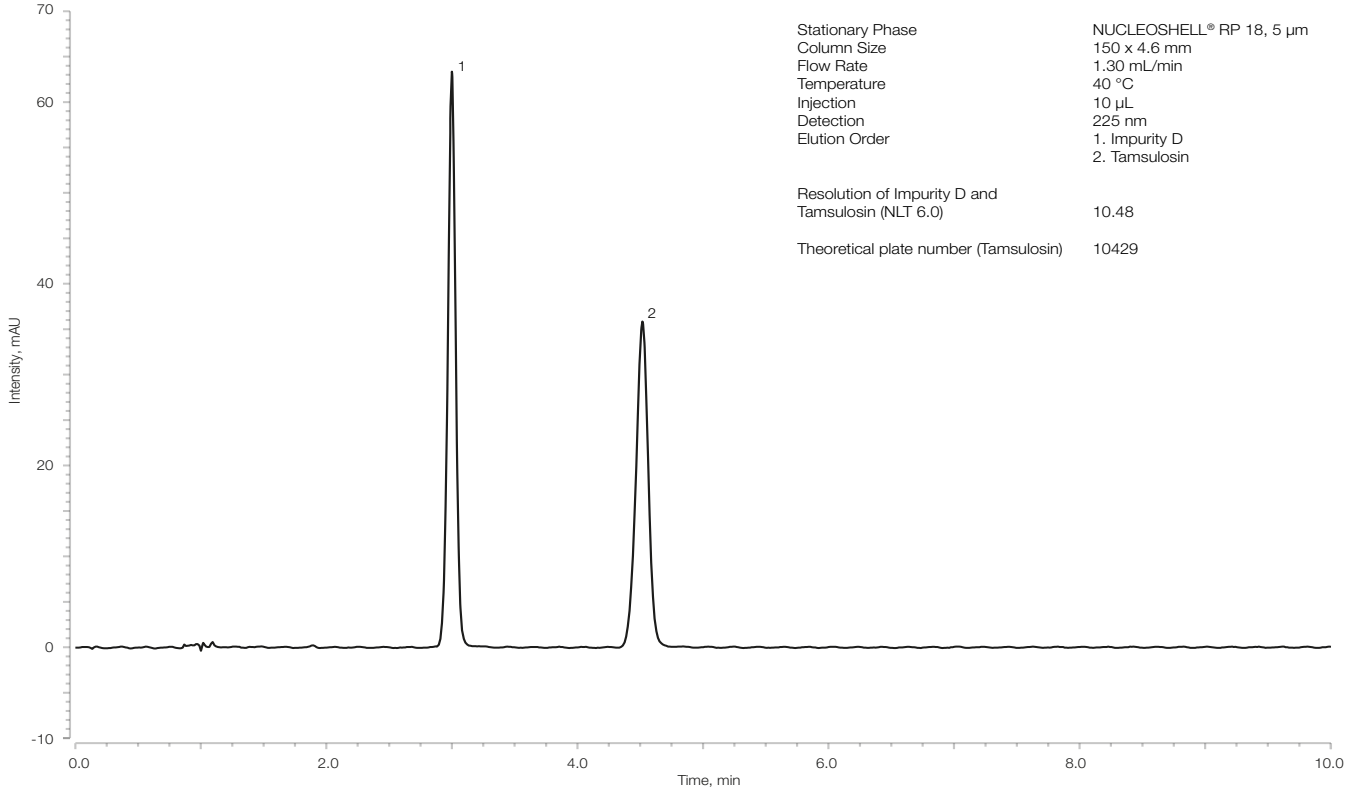


Figure 2: b

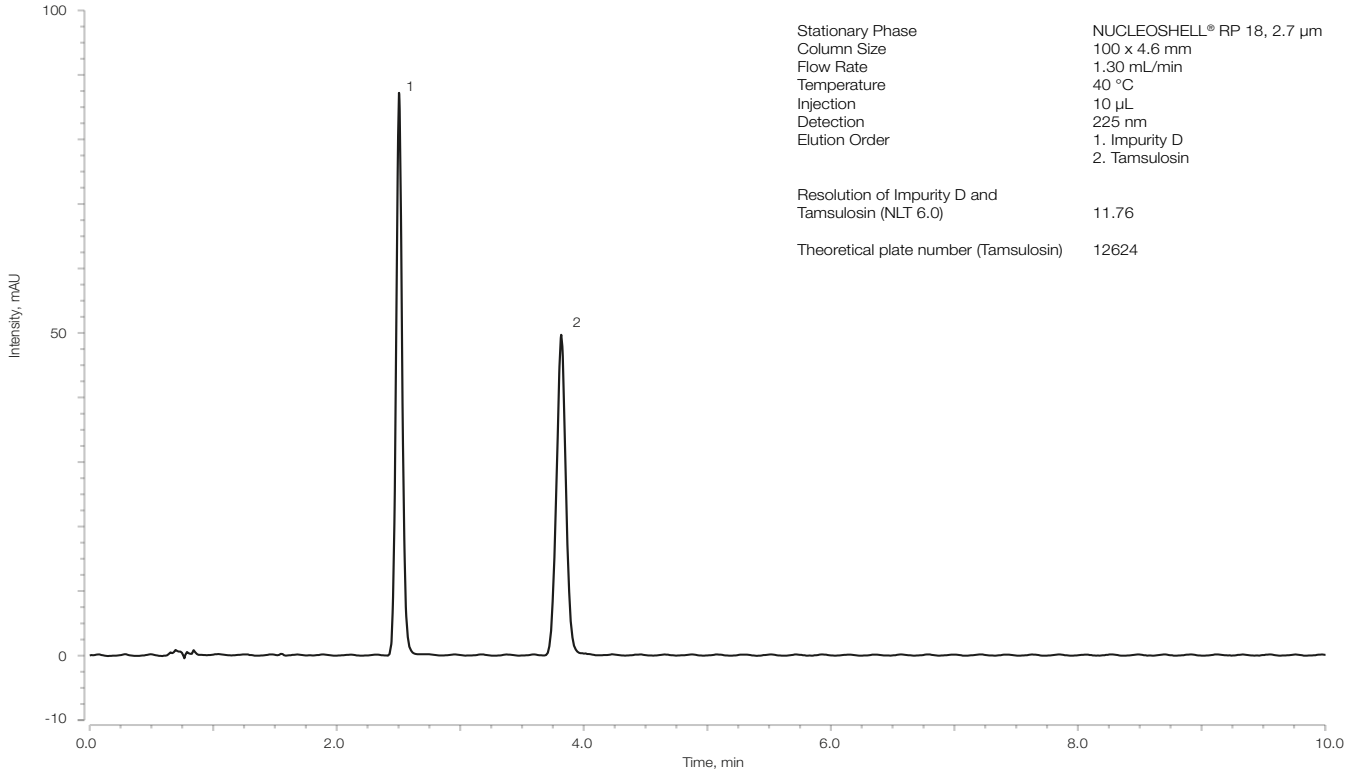
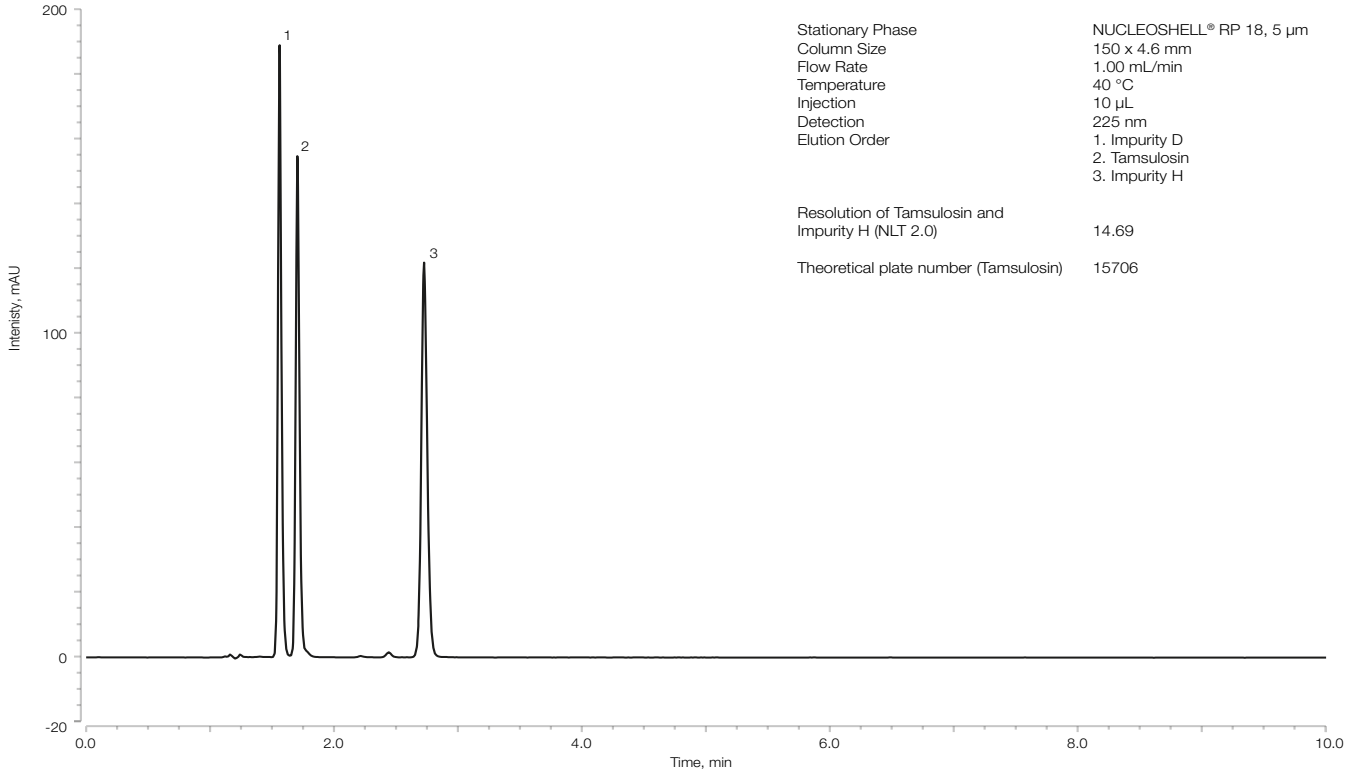


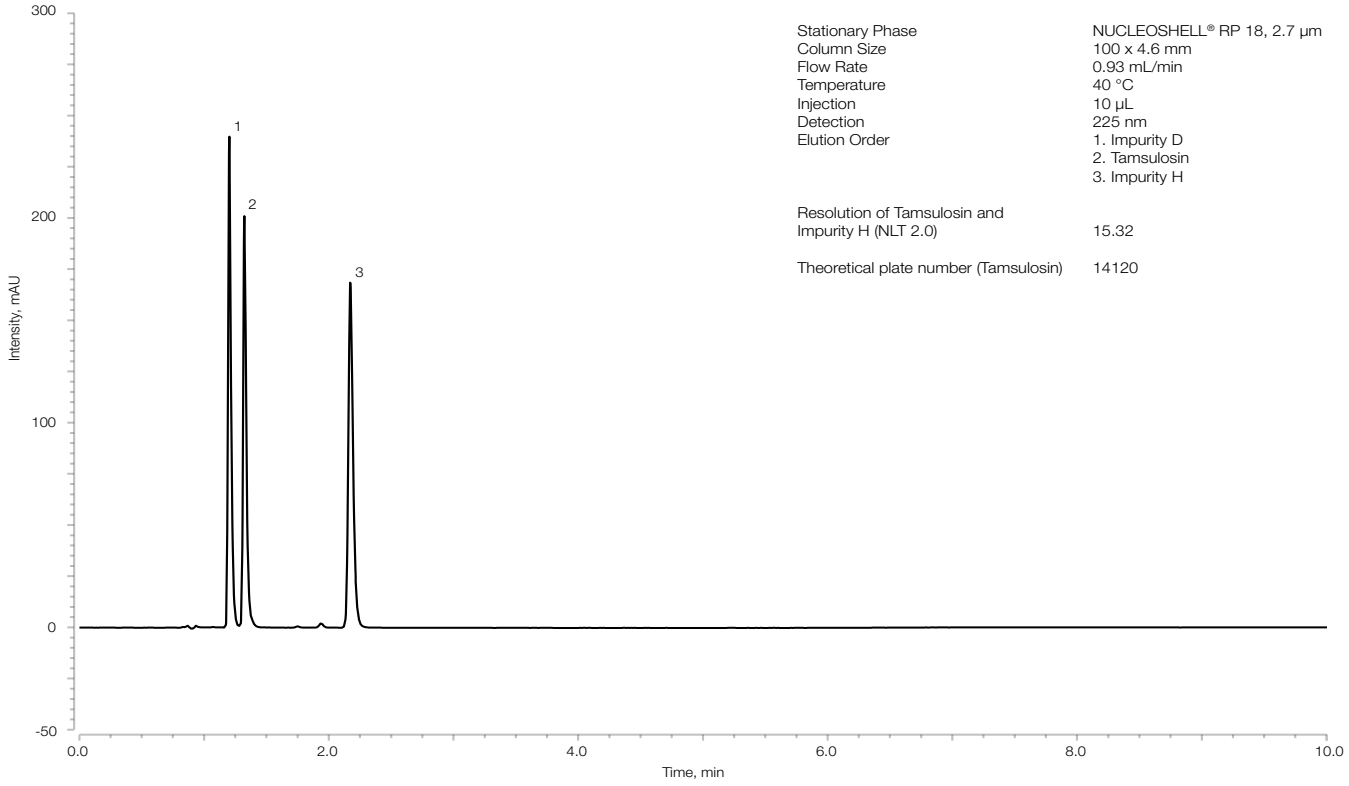
Figure 2: a: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 5 µm, 150x4.6 mm, b: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 2.7 µm, 100x4.6 mm

Figure 3: a



Stationary Phase	NUCLEOSHELL® RP 18, 5 µm
Column Size	150 x 4.6 mm
Flow Rate	1.00 mL/min
Temperature	40 °C
Injection	10 µL
Detection	225 nm
Elution Order	1. Impurity D 2. Tamsulosin 3. Impurity H
Resolution of Tamsulosin and Impurity H (NLT 2.0)	14.69
Theoretical plate number (Tamsulosin)	15706

Figure 3: b



Stationary Phase	NUCLEOSHELL® RP 18, 2.7 µm
Column Size	100 x 4.6 mm
Flow Rate	0.93 mL/min
Temperature	40 °C
Injection	10 µL
Detection	225 nm
Elution Order	1. Impurity D 2. Tamsulosin 3. Impurity H
Resolution of Tamsulosin and Impurity H (NLT 2.0)	15.32
Theoretical plate number (Tamsulosin)	14120

Figure 3: a: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 5 µm, 150x4.6 mm, b: EC HPLC column (analytical), NUCLEOSHELL® RP 18, 2.7 µm, 100x4.6 mm

Results (a)

Method Parameter	Allowed Adjustments (isocratic elution)*	Method 1	Method 2
Mobile phase pH	± 0.2 units	As specified	As specified
Concentration of salts in buffer	± 10%	As specified	As specified
Composition of the mobile phase	± 30% of the minor solvent component relative or 2% absolute, whichever is the larger. No other component is altered by more than 10% absolute.	As specified	As specified
Stationary phase	No change of C18 allowed	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	100 mm / 2.7 µm (+ 23.5%*)
Column internal diameter	± 25%	4.6 mm as specified	4.6 mm as specified
Flow Rate	± 50% after adjustment due to a change in column dimensions	1.30 mL/min as specified	1.20 mL/min (± 0% after adjustments)
Column temperature	± 10 °C	25 °C as specified	25 °C as specified
Injection volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory	10 µL as specified	10 µL as specified
Detection [nm]	No change permitted	225 nm as specified	225 nm as specified
Retention time (Tamsulosin)		4.538 min	3.814 min (– 16.0%**)
Theoretical plate number (Tamsulosin)	Within – 25% to 50%, relative to the prescribed column***	10429	12624 (+ 21.0%**)
System suitability requirements Resolution:	NLT 6.0 between Impurity D and Tamsulosin	10.48	11.76

* Change in comparison to European Pharmacopeia 11.0, Chapter 2.2.46. Chromatographic separation techniques
** Change in comparison to method 1
*** Column used in method 1

Results (b)

Method Parameter	Allowed Adjustments (isocratic elution)*	Method 1	Method 2
Mobile phase pH	± 0.2 units	As specified	As specified
Concentration of salts in buffer	± 10%	As specified	As specified
Composition of the mobile phase	± 30% of the minor solvent component relative or 2% absolute, whichever is the larger. No other component is altered by more than 10% absolute.	As specified	As specified
Stationary phase	No change of C18 allowed	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	100 mm / 2.7 µm (+ 23.5%*)
Column internal diameter	Can be adjusted so long as linear velocity is maintained	4.6 mm as specified	4.6 mm as specified
Flow Rate	± 50% after adjustment due to a change in column dimensions	1.00 mL/min as specified	0.93 mL/min (– 50.0% after adjustments)
Column temperature	± 10 °C	25 °C as specified	25 °C as specified
Injection volume	May be decreased, provided detection and repeatability of the peak(s) to be determined are satisfactory	10 µL as specified	10 µL as specified
Detection [nm]	No change permitted	225 nm as specified	225 nm as specified
Retention time (Tamsulosin)		1.709 min	1.326 min (– 22.4%**)
Theoretical plate number (Tamsulosin)	Within – 25% to 50%, relative to the prescribed column***	15706	14120 (– 10.4%**)
System suitability requirements Resolution:	NLT 2.0 between Tamsulosin and Impurity H	14.69	15.32

* Change in comparison to European Pharmacopeia 11.0, Chapter 2.2.46. Chromatographic separation techniques
** Change in comparison to method 1
*** Column used in method 1

Conclusion

The superficially porous NUCLEOSHELL® RP 18, 5 µm, 150x4.6 mm HPLC column from MACHEREY NAGEL fulfills all requirements of the Ph. Eur. monograph 2131. Further method development leads to shorter runtimes ((a) – 16.0% (b) – 22.4%) and lower solvent consumption, optimizing the analysis of Tamsulosin with regard to the guidelines of green chemistry. We were also able to improve the resolution as well as the peak intensity, while keeping all method parameters well within the allowed adjustment range of the European Pharmacopeia.

The chromatography application database

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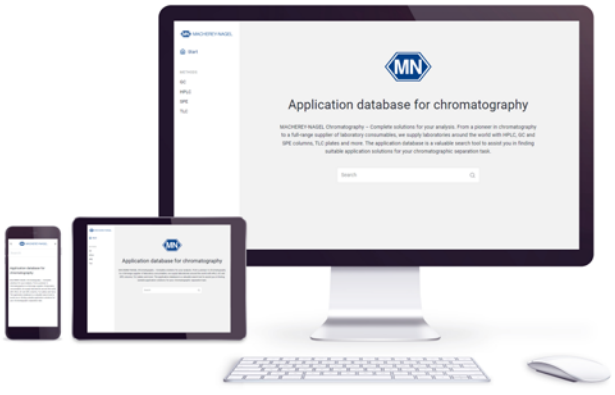
- Free access to the MN application database: *https://chromaappdb.mn-net.com*



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