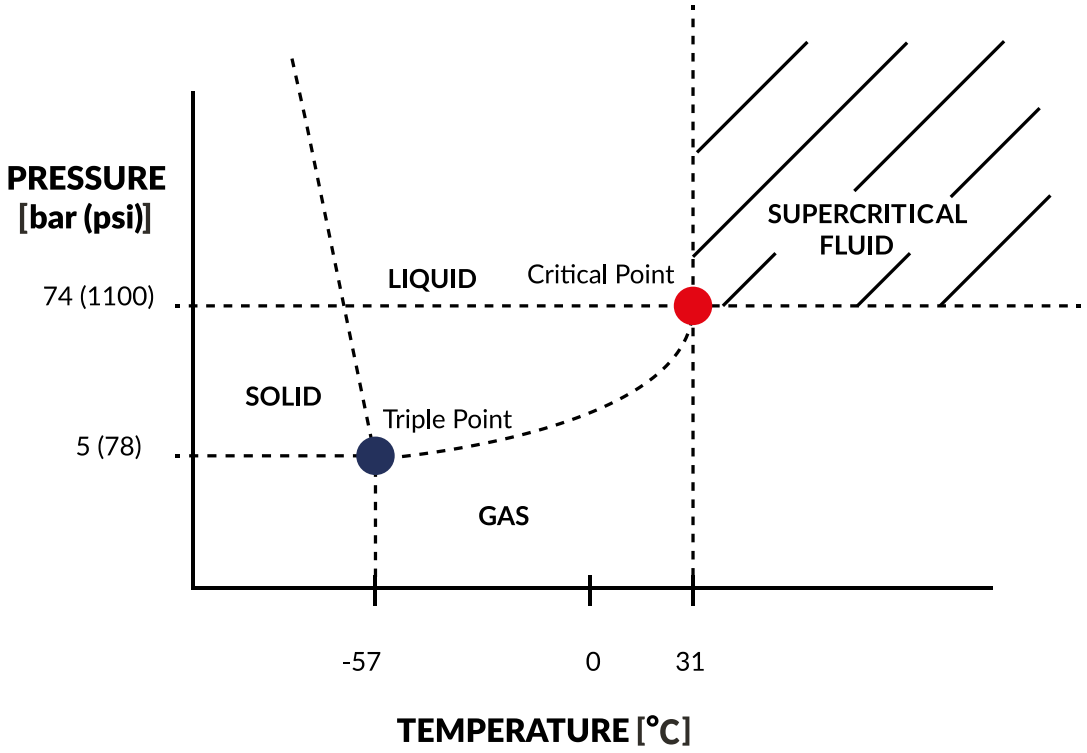
Dr. Maisch

Any Column, Any Size, Any Media



SFC COLUMNS

for Achiral, Chiral and SEC Applications

MADE BY DR. MAISCH

CONTENT

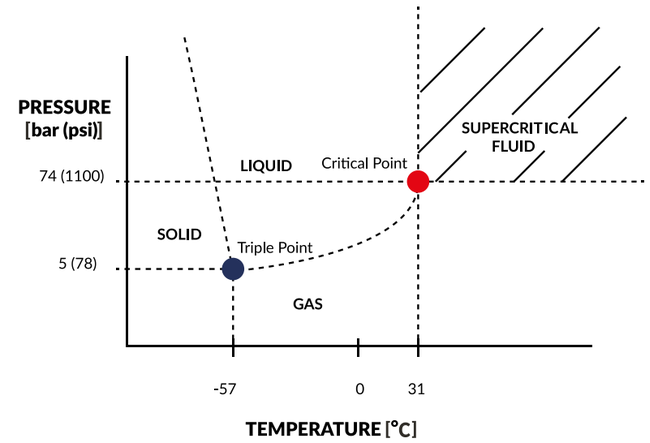
SFC COLUMNS MADE BY DR. MAISCH

From one of the biggest

High-**P**erformance **L**iquid **C**hromatography (HPLC) and

Ultra **H**igh-**P**erformance **L**iquid **C**hromatography (UHPLC)

Column Manufacturers in Europe.



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INTRODUCTION

Supercritical Fluid Chromatography (SFC) is a chromatographic technique using supercritical carbon dioxide (CO_2) as mobile phase. Supercritical CO_2 can be mixed with alcohols (despite its low polarity).

The developpment process for analytical SFC methods is basically the same as for analytical HPLC methods. SFC can be used to analyze any compound that is compatible with supercritical carbon dioxide and can be dissolved in an organic solvent.

The following resolution equation for HPLC is also valid for SFC:

$$R_s = 1/4\sqrt{N} \cdot \frac{\alpha-1}{\alpha} \cdot \frac{k}{1+k}$$

Efficiency Selectivity Retention

Figure 1: Resolution Quotation for HPLC and SFC (Rs: Resolution, N: Efficiency, α: Selectivity, k: Capacity Factor).

The Efficiency N, Selectivity α, Capacity Factor k affect the Resolution Rs and are all independent factors depending on:

- Column Dimension.
- Mobile Phase.

Separation can be improved by increasing N and α if a minimum of retention exists.

Resolution - Optimizing Efficiency

The particle size of the silica media directly impacts the efficiency, as measured by the number of theoretical plates (N). A smaller particle size improves the efficiency of a separation.

Dr. Maisch offers a wide variety of particle sizes across its different product lines. In Table 1 you can find the standard Reprospher phases used for SFC applications.

RESOLUTION

OPTIMIZING EFFICIENCY

Table 1: Available Particle Sizes of the standard Reprospher Phases used for SFC Applications.

Increasing Efficiency and Backpressure

	Particle Size and Part Number (PN)					
Media	**1.7 µm**	**1.8 µm**	**2 µm**	**2.5 µm**	**3 µm**	**5 µm**
Reprospher 100 Si	rs117.00	rs118.00	rs12.00	rs125.00	rs13.00	rs15.00
Reprospher 100 NH2 not endc.	N/A	N/A	N/A	N/A	rs13.a0	rs15.a0
Reprospher 100 NH2-DE	N/A	rs118.ade	rs12.ade	N/A	N/A	rs15.ade
Reprospher 100 CN	N/A	rs118.c0	rs12.c0	rs125.c0	rs13.c0	rs15.c0
Reprospher 100 CN-DE	rs117.cde	rs118.cde	N/A	N/A	N/A	rs15.cde
Reprospher 100 Diol-DE	N/A	N/A	N/A	N/A	N/A	rs15.dde
Reprospher 100 Diol	N/A	N/A	N/A	N/A	rs13.d0	rs15.d0

The backpressure generated by the SFC system limits the particle size that can be used. Scale-Up in SFC applications is more complex compared to HPLC conditions due to the compressibility of CO_2 causing density, pressure and temperature variations.

These variations have an impact on the mobile phase (retention, selectivity). This complicates the scale-up process from analytical to preparative methods. Most stationary phases used for SFC applications are not endcapped. A higher silica surface increases the retention. On the other side such non-endcapped columns show a shorter lifetime.

Another approach to achieve higher efficiencies is to change the design of the silica particle from fully-porous to core-shell particles. Core-shell particles exhibit very high efficiency relative to fully porous particles of equivalent diameter. Table 2 shows examples of ReproShell Media offered by Dr. Maisch, which are based on core-shell particles.

Table 2: Available ReproShell Media.

	Particle Size and Part Number (PN)	
Media	**2.7 µm**	**5 µm**
ReproShell ODS-1	cs27.91	cs15.91
ReproShell ODS-3	cs27.93	cs15.93
ReproShell Si	cs27.00	cs15.00
ReproShell PFP	cs27.pfp	cs15.pfp
ReproShell Phenyl-Hexyl	cs27.ph	cs15.ph
ReproShell C8	cs27.8e	cs15.8e
ReproShell Biphenyl	cs27.bpe	cs15.bpe

Resolution - Optimizing Mobile Phase

CO_2 is not polar enough for the elution of polar compounds. The addition of a polar organic co-solvent (modifier) is necessary to allow elution and to have reasonable run times. Supercritical CO_2 is completely miscible with all commonly used organic solvents.

When mixed with an organic modifier, the critical point of CO_2 is changing, bringing the mobile phase in a state that is not necessarily supercritical anymore.

Increasing the concentration of the organic modifier in the mobile phase:

- Increases the eluotropic strength.
- Decreases the retention times.

The modifier can also be adsorbed at the surface of the stationary phase, leading to a modification of this surface.

The choice of the modifier depends on:

- Eluent strength.
- Selectivity.
- Efficiency.
- Peak shapes achieved in initial test runs.

Bad peak shapes can be minimized by the addition of an organic modifier with H-bond donor capacity (MeOH, EtOH, IPA).

List of Potential Modifiers

- **Alcohols** - MeOH is by far the most commonly used alcohol in SFC applications, due to its ability to achieve higher separation efficiency and shorter analysis times in comparison to EtOH and IPA.
  - Highest eluotropic strength.
  - Efficiency: MeOH > EtOH > IPA
  - High polarity favors solubility of compounds in the mobile phase.
  - MS-detection is more sensitive (lower surface tension of MeOH gives better ionization compared to other alcohols).

RESOLUTION
OPTIMIZING MOBILE PHASE

- **Acetonitrile (ACN)**
  - Unique and different selectivity.
  - Aprotic solvent.
  - Poor chromatographic performance (very low efficiency, bad peak shapes).

- **Mix of Methanol and Acetonitrile**
  - Improves selectivity without altering peak shape.

- **Acidic Additives** (Formic Acid, Acetic Acid, Trifluoroacetic Acid (TFA), Citric Acid)
  - Improves the peak shapes of strong acids.

- **Basic Additives** (Isopropylamine, Diethylamine, Ethyldimethylamine, or Triethylamine)
  - Improves the peak shape of strong bases.

In the presence of both acidic and basic compounds in the sample, it is possible to include an acidic and a basic additive in the modifier.

- **Volatile Additives** (Ammonium Hydroxide, Ammonium Acetate or Ammonium Formate)
  - Improve the peak shape of acidic and basic compounds. These are compatible with **MS-detection** and easier to evaporate in the preparative scale.
  - Water is not fully soluble in CO_2 but it can be mixed in a reasonable proportion (1–5%) to a CO_2–MeOH mobile phase, in addition or replacement of traditional additives to improve the peak shape.

Most additives absorb in the UV range, leading to a baseline drift using a gradient method. Therefore, there is significant interest in stationary phases that provide symmetrical peaks without the need for additives in the mobile phase.

COLUMNS MADE BY DR. MAISCH 7

In the Reversed-Phase (RP) HPLC world a C18 modified Silica Column would typically be the starting point for the method development process. In achiral SFC applications, the use of C18 columns is theoretically possible, but in practice, the success rate is very low.

Various achiral columns used in HPLC applications can also be used for SFC applications. However, it is really difficult to predict the behaviour of a silica modification and also completely different silica modifications often provide superior separations.

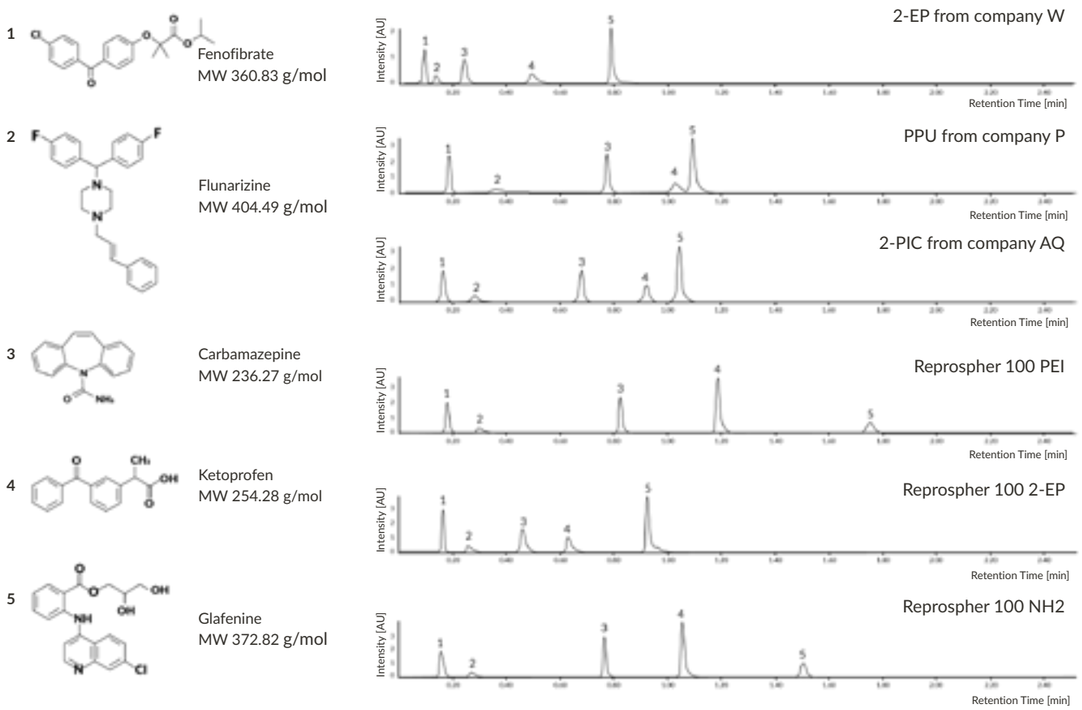

Figure 2: Testmix of 5 Compounds on 6 differents SFC Columns. Application Courtesy of John Reilly, Norvartis Institut of Biomedical Research NiBr AG Basel, 4002 Basel, Switzerland.

Column:	Analytical SFC Columns
Dimension:	50 x 3 mm
Mobile Phase:	A: CO_2
	B: MeOH or MeOH + 0.1% Basic Modifier
Temperature:	35 °C

Several stationary phases from Dr. Maisch exhibit excellent performance used in SFC applications. The most successful phase is Reprospher Polyethyleneimine (PEI).

REPROSPHER POLYETHYLENEIMINE (PEI)

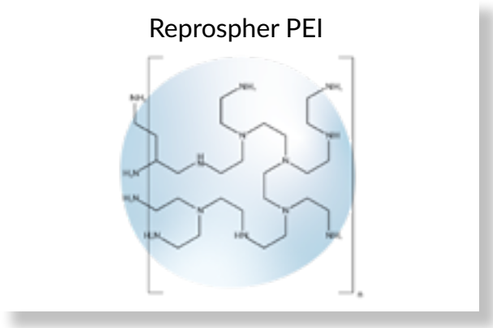

Figure 3: Scheme of Reprospher PEI.

Reprospher PEI exhibits a higher density of amino groups compared to traditional amino phases (factor 3). The polymer skeleton includes primary, secondary and tertiary amine groups.

Table 3: Available Reprospher PEI Media.

			Particle Size and Part Number (PN)				
Media	**Modification**	**Pore Size [Å]**	**3 µm**	**5 µm**	**10 µm**	**30 µm**	**50 µm**
Reprospher 100 PEI	Polyethyleneimine	100	rs13.pei	rs15.pei	rs10.pei	rs130.pei	rs150.pei
Reprospher 300 PEI	Polyethyleneimine	300	rs33.pei	rs35.pei	rs30.pei	N/A	N/A

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Superior Performance of Reprospher PEI

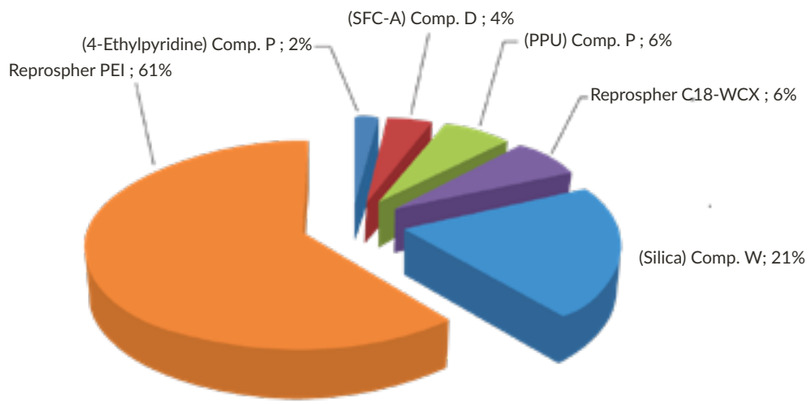

Figure 4: Superior Performance of Reprospher PEI.

Published by: Thomas Wolf, Alexander Marzlale, Eric Francotte and Trixie Wagner
Achiral SFC-MS Lab: Support of Global Discovery Chemistry Basel 2016

SFC COLUMNS FOR ACHIRAL APPLICATIONS
REPROSPHER PEI

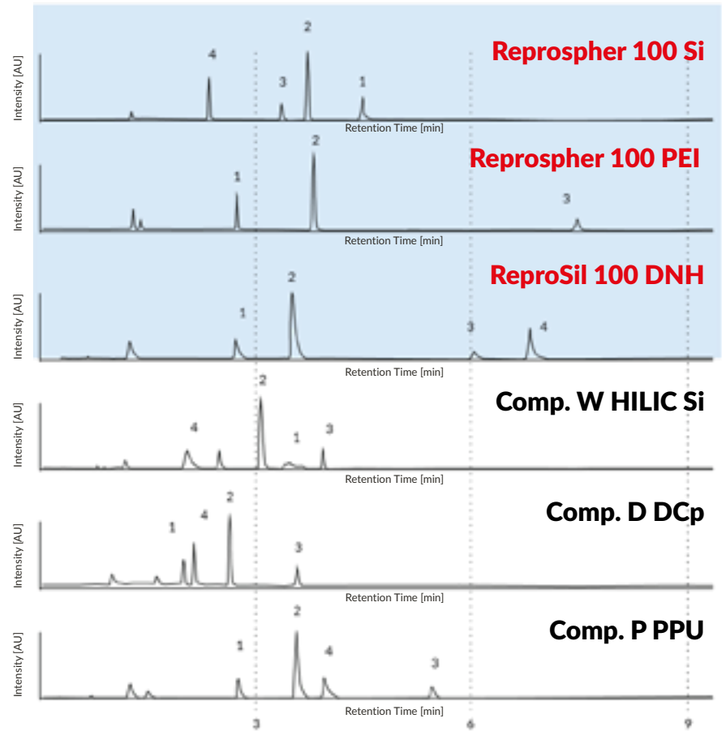

Figure 5: Testmix of 4 different Compounds on 6 different SFC Columns. Application Courtesy of Eric Francotte, Novartis AG, 8th International Conference on Packed Column SFC, Oct 2014, Basel, Switzerland.

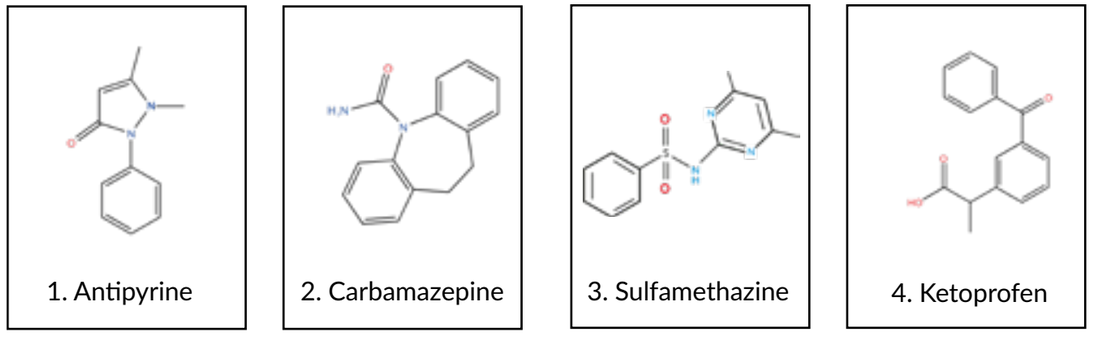

Figure 6: The 4 Compounds of the used Testmix.

Column:	Analytical SFC Columns
Dimension:	250 x 4.6 mm
Mobile Phase:	CO_2 + MeOH (5-50% in 6 min)
Flow Rate:	1.0 ml/min
Detection:	UV-Detection @254 nm

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Reprospher HILIC-ARG

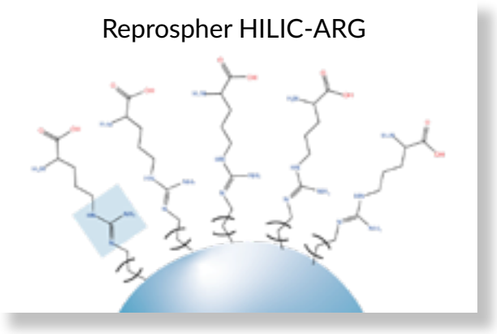


Figure 7: Scheme of Reprospher HILIC-ARG.

Table 4: Available Reprospher HILIC-ARG Media.

			Particle Size and Part Number (PN)	
Media	**Modification**	**Pore Size [Å]**	**3 µm**	**5 µm**
Reprospher HILIC-ARG	Arginine	100	rs13.ARG	rs15.ARG

Reprospher HILIC-ARG is a silica phase surface modified with arginine and exhibits acidic and basic functionality. The phase has a strong affinity to hydrophilic compounds and offers a very special selectivity compared to other SFC phases.

ReproSil CBD

Special phase for cannabinoids: CBD purification.

Perfect resolution for Cannabidiol (CBD) and Cannabigerol (CBG) isolation from other cannabinoids.

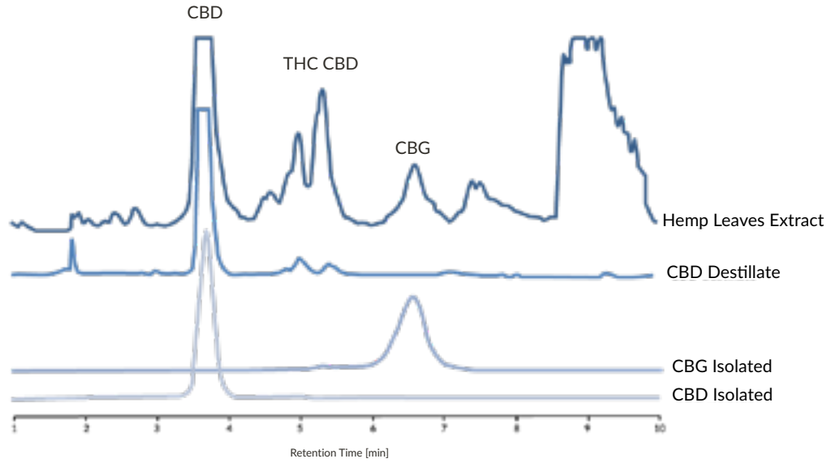
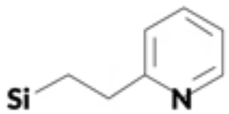


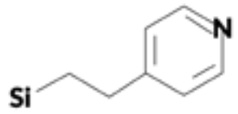
Figure 8: Hemp Leaves Extract, CBD Destillate, CBG Isolated and CBD Isolated.

Column: ReproSil CBD
Dimension: 250 x 4.6 mm
Mobile Phase: 4% MeOH
Detection: UV-Detection @220 nm

REPROSPHER 2-EP AND 4-EP



Reprospher 2-Ethylpyridine (2-EP)



Reprospher 4-Ethylpyridine (4-EP)

Figure 9: Scheme of Reprospher 2-EP and 4-EP.

Table 5: Available Reprospher 2-EP and 4-EP Media.

			Particle Size and Part Number (PN)		
Media	**Modification**	**Pore Size [Å]**	**3 µm**	**5 µm**	**10 µm**
Reprospher 100 2-EP	2-Ethylpyridine	100	rs13.2ep	rs15.2ep	rs10.2ep
Reprospher 100 4-EP	4-Ethylpyridine	100	N/A	rs15.4ep	rs10.4ep

Ethylpyridine (EP) modified silica has been the gold standard for achiral SFC analysis of basic compounds for a long time because these phases generally do not require an addition of amines to the eluent, still giving excellent peak shape and reproducibility.

The pyridine group minimizes interactions with silanol groups by steric shielding. EP-phases are also useful phase for the separation of neutral and acidic polar compounds.

The 4-EP phase offers alternative selectivity to the 2-EP phase.

Reprospher C18-WCX

Reprospher C18-WCX

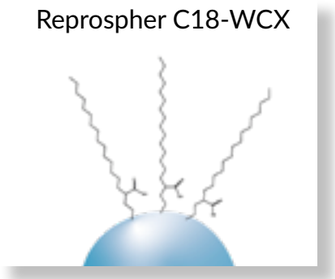


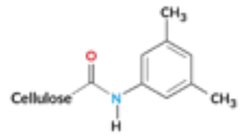
Figure 10: Scheme of Reprospher C18-WCX.

Table 6: Available Reprospher C18-WCX Media.

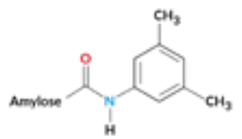
			Particle Size and Part Number (PN)		
Media	**Modification**	**Pore Size [Å]**	**3 µm**	**5 µm**	**10 µm**
Reprospher 100 C18-WCX	C18 + Carboxylic Acids	100	rs13.9ac	rs15.9ac	rs10.9ac

This mixed mode phase combines a carboxylic group directly connected to a hydrophobic C18 chain. This media is non-endcapped and allows multiple interactions which result in special selectivity.

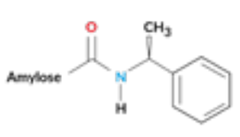
REPROSIL CHIRAL



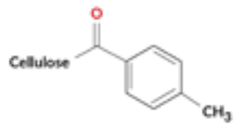
ReproSil Chiral-OM
(Chiralcel-OD, Lux Cellulose-1)



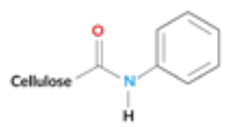
ReproSil Chiral-AM
(Chiralpak AD, Lux Amylose-1)



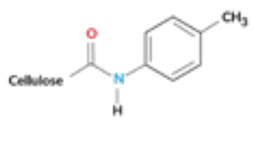
ReproSil Chiral-AMS
(Chiralpak AS)



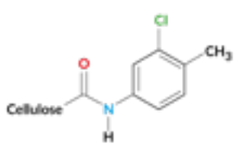
ReproSil Chiral-JM
(Chiralcel-OJ, Lux Cellulose-3)



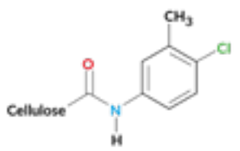
ReproSil Chiral-CM
(Chiralcel-OC)



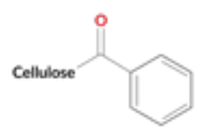
ReproSil Chiral-GM
(Chiralcel-OG)



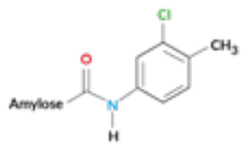
ReproSil Chiral-ZM
(Chiralcel-OZ, Lux Cellulose-2)



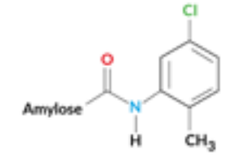
ReproSil Chiral-XM
(Chiralcel-OX, Lux Cellulose-4)



ReproSil Chiral-BM
(Chiralcel-OB)



ReproSil Chiral-ZA
(Chiralpak AZ)



ReproSil Chiral-YM
(Chiralpak AY, Lux Amylose-2)

Figure 11: ReproSil Chiral Phases.

ReproSil Chiral OM, CM, JM, ZM, BM, AM, AMS, ZA and YM Phases are prepared by coating the silica with a polysaccharide (e.g. cellulose or amylose). Therefore, the presence of any solvent capable of dissolving polysaccharides must be strictly avoided, even at trace levels.

- Ethers incl. THF, Acetone, Chlorinated Solvents, Ethyl Acetate, DMSO, DMF, N-Methyl-formamide, Toluene, Ketones, Dimethylacetamide
- IPA > 50%

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Coated Dr. Maisch Chiral Phases as Alternatives to Chiral Phases from Daicel and Phenomenex

The Dr. Maisch polysaccharide phases are excellent alternatives to existing Daicel phases which was confirmed by many happy Dr. Maisch customers globally and mentioned in several scientific publications in the scientific world. One example:

EVALUATION OF REPROSIL CHIRAL-OM VS. OD

Evaluation of a silica phase modified with cellulose tris(3,5-dimethylphenylcarbamate) „ReproSil Chiral-OM“ in supercritical fluid chromatography. Syame Khater and Caroline West, University of Orleans, CNRS UMR 7311, ICOA.

All experiments were performed on a Jasco SFC system and an Acquity UPC² system. ReproSil Chiral-OM is based on silica coated with cellulose tris(3,5-dimethylphenylcarbamate). Two hundred and thirty achiral compounds and one hundred and thirty chiral racemic compounds were screened on different polysaccharide-type chiral stationary phases in SFC using the following operating conditions: CO_2/MeOH 90:10, flow rate 3 ml/min, oven temperature 25 °C, outlet pressure 150 bar.

NON-SPECIFIC INTERACTIONS AND RETENTION

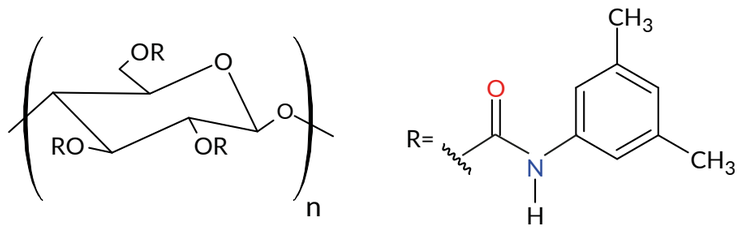

Figure 12: Scheme of cellulose tris(3,5-dimethylphenylcarbamate).

Retention on cellulose tris(3,5-dimethylphenylcarbamate) could be explained by non-specific interactions such as π-π interactions, hydrogen bonding and stereo-induced interactions.

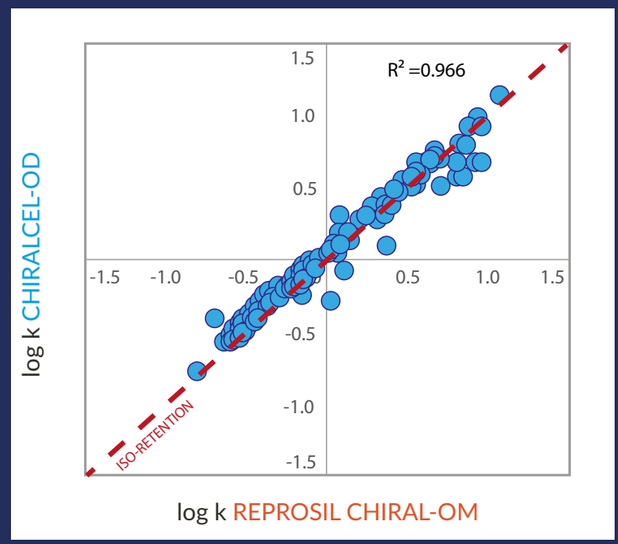

Figure 13: log k Chiralcel-OD vs. log k ReproSil Chiral-OM.

The investigation on non-specific interactions that control retenton is based on the analysis of 230 achiral compounds.

The k-k plot on the left compares the logarithms of retention factors of 168 achiral species on Chiralcel-OD vs. ReproSil Chiral-OM. The phases are expected to be similar since they possess the same chiral selector (R^2 =0.966). They would provide similar non-specific interactions.

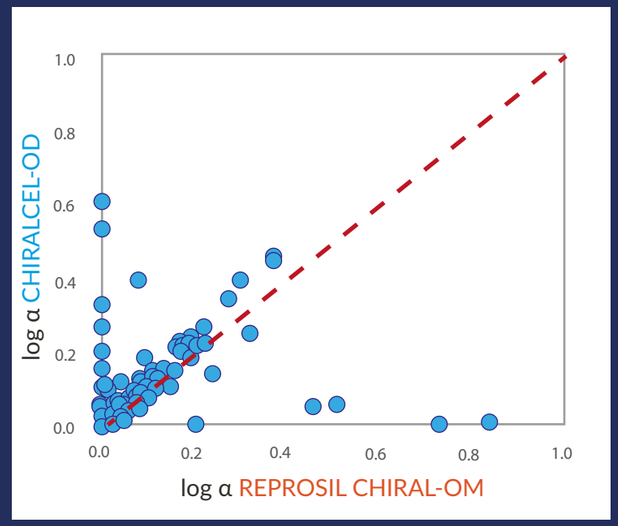

Figure 14: log α Chiralcel-OD vs. log α ReproSil Chiral-OM.

The α-α plot below compares the logarithm of separation factors measured for 130 racemates on Chiracel-OD vs. ReproSil Chiral-OM.

The major part of the compounds is located on the dotted line, indicating similar separation behaviour of the two columns.

Chiralcel-OD provides a higher number of unique hits. Indeed, 81% of the tested chiral species are resolved on ReproSil Chiral-OM against 86% on Chiralcel-OD. However, some racemates are well separated on ReproSil Chiral-OM with little or no separation on Chiralcel-OD.

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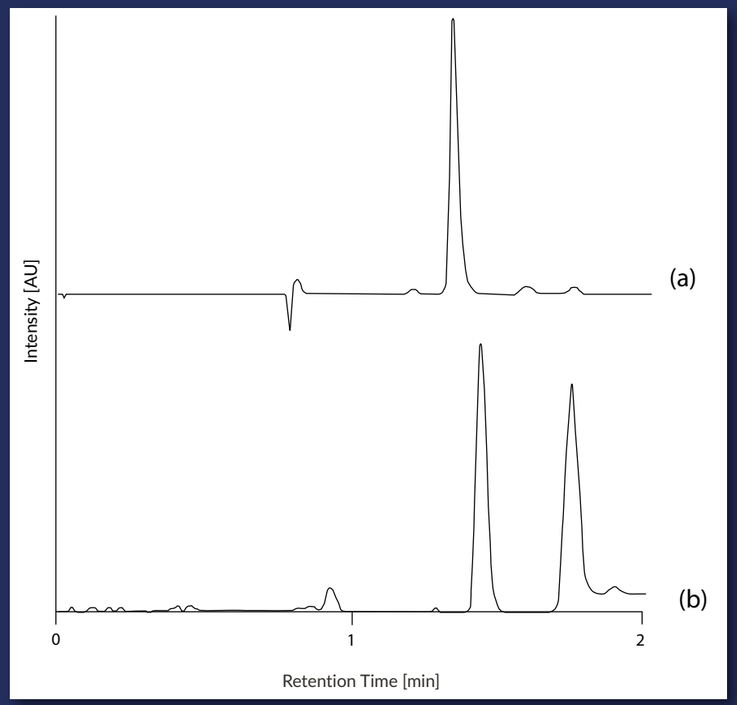
The following chromatograms illustrate the complementary of the generic phases having cellulose tris(3,5-dimethylphenylcarbamate) as chiral selector in the course of method development: Chiralcel-OD vs. ReproSil Chiral-OM. The chromatograms illustrate that the chiral (2,3-Epoxypropyl)-benzene is well resolved on ReproSil Chiral-OM (b) but there is no separation on Chiralcel-OD (a).



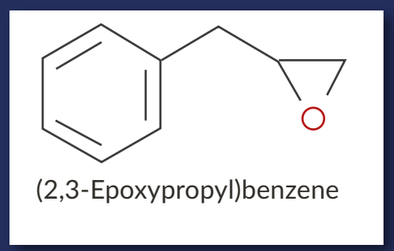


Figure 15: Separation of (2,3-Epoxypropyl)benzene on Chiralcel-OD (a) and ReproSil Chiral-OM (b).

SFC COLUMNS FOR CHIRAL APPLICATIONS
REPROSIL CHIRAL

Comparison of ReproSil Chiral-OM and Chiralcel-OD

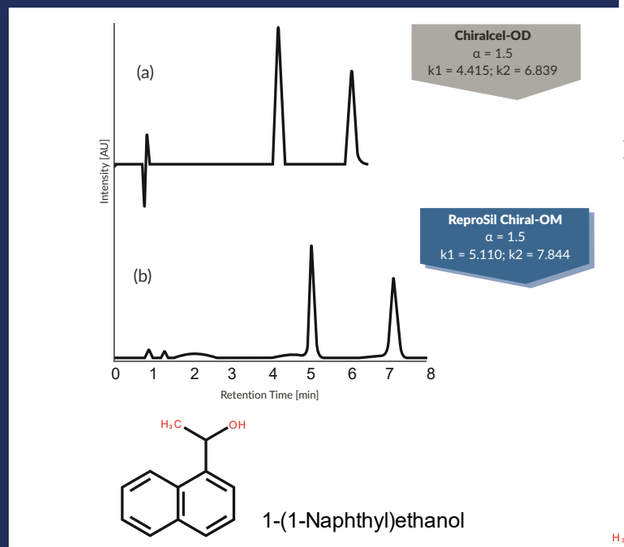


Figure 16: Separation of 1-(1-Naphthyl)ethanol on Chiralcel-OD (a) and ReproSil Chiral-OM (b).

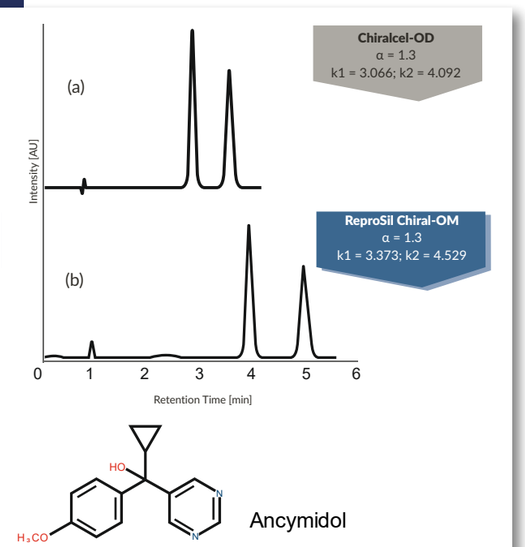


Figure 17: Separation of Ancymidol on Chiralcel-OD (a) and ReproSil Chiral-OM (b).

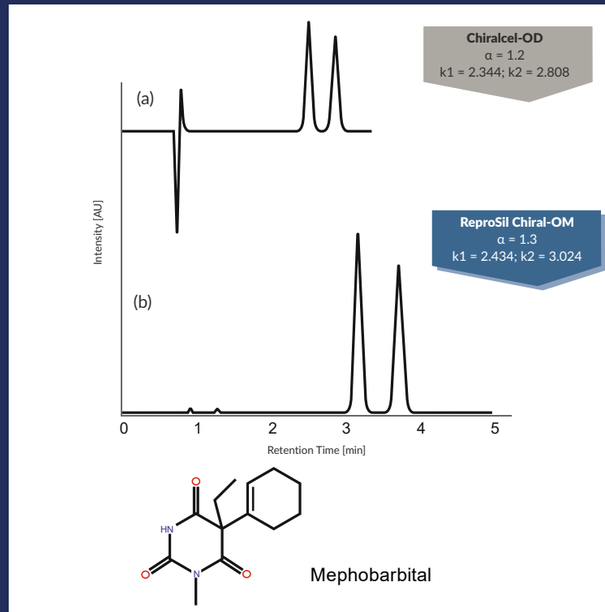


Figure 18: Separation of Mephobarbital on Chiralcel-OD (a) and ReproSil Chiral-OM (b).

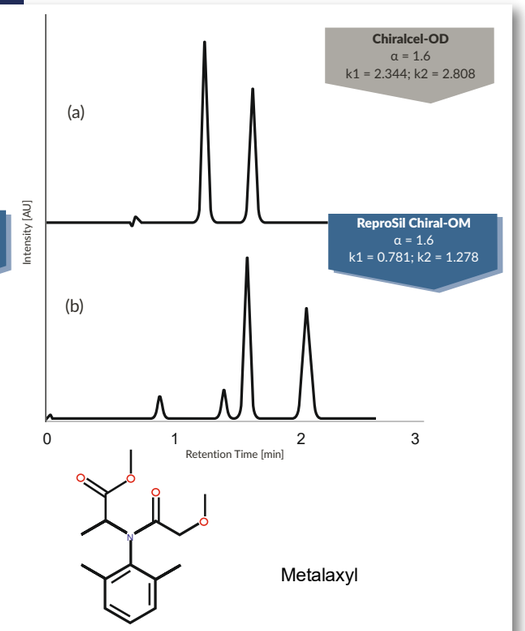


Figure 19: Separation of Metalaxyl on Chiralcel-OD (a) and ReproSil Chiral-OM (b).

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The analysis of Fenamiphos, Gluthetimide and 5-Methyl-5-phenylhydantoin on ReproSil Chiral-OM provide a better starting point for a method development than those on RegisCell, Lux Cellulose-1 or Cellucoat, respectively.

NO SEPARATION

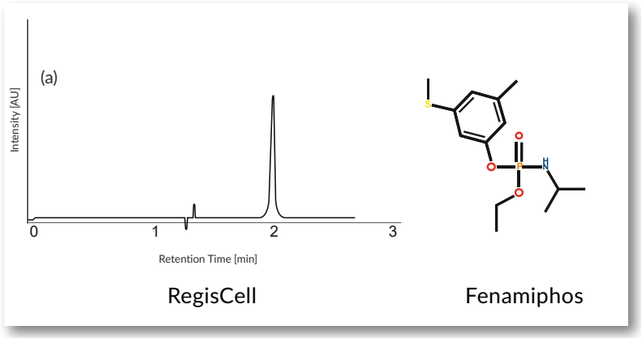


Figure 20: Separation of Fenamiphos on RegisCell (a) and ReproSil Chiral-OM (b).

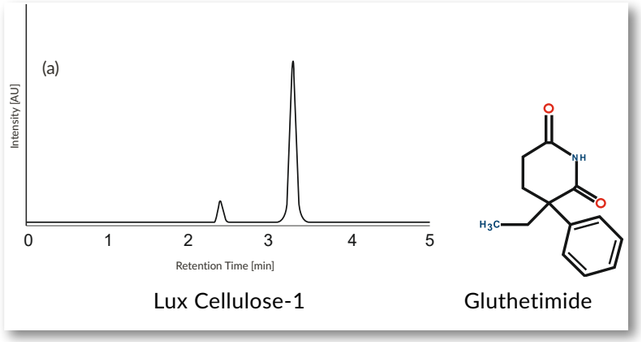


Figure 21: Separation of Gluthetimide on Lux Cellulose-1 (a) and ReproSil Chiral-OM (b).

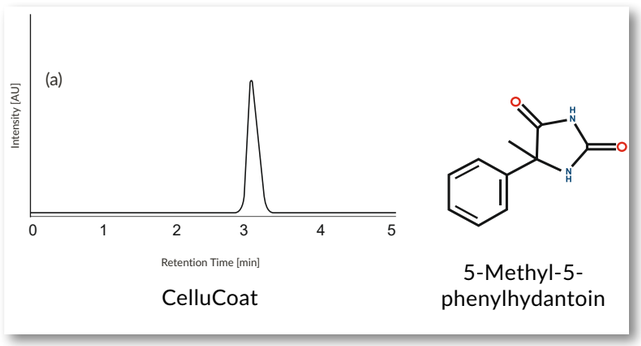
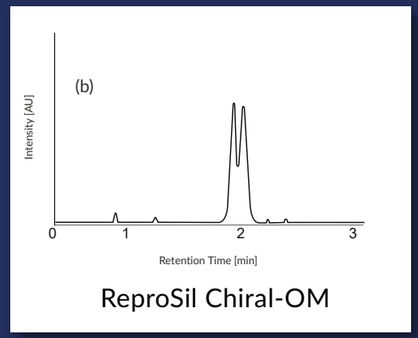
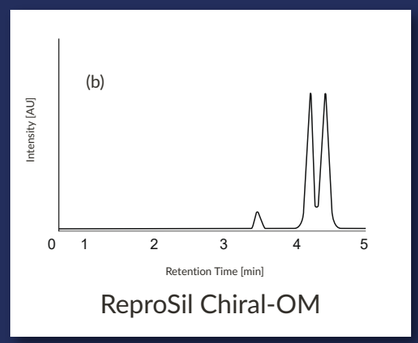
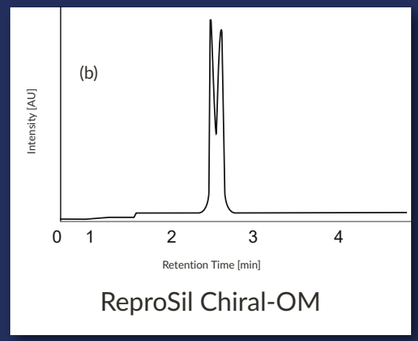


Figure 22: Separation of 5-Methyl-5-phenylhydantoin on CelluCoat (a) and ReproSil Chiral-OM (b).

SEPARATION







ReproSil Chiral-OM and Chiralcel OD-H

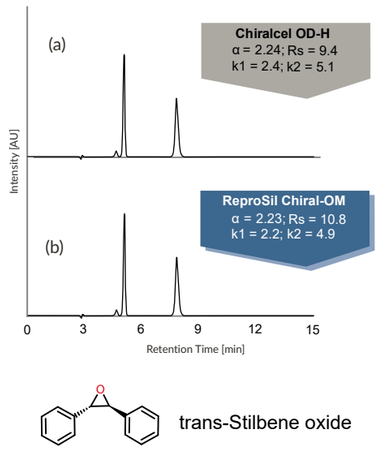


Figure 23: Separation of trans-Stilbene oxide on Chiralcel OD-H (a) and ReproSil Chiral-OM (b).

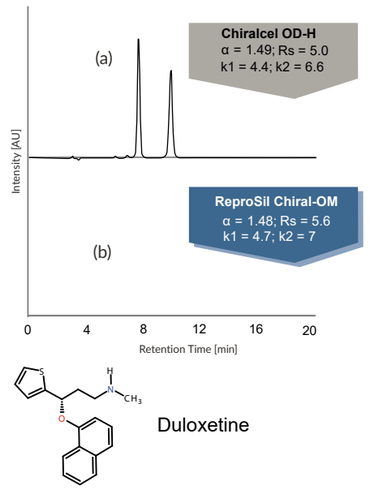


Figure 24: Separation of Duloxetine on Chiralcel OD-H (a) and ReproSil Chiral-OM (b).

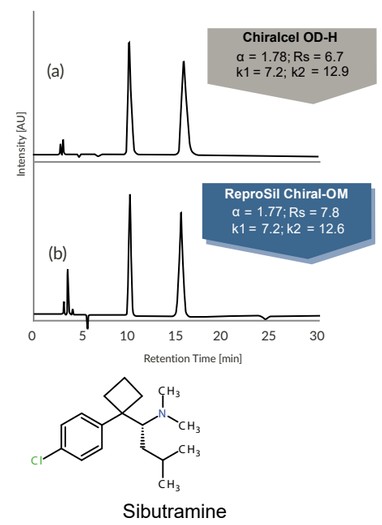


Figure 25: Separation of Sibutramine on Chiralcel OD-H (a) and ReproSil Chiral-OM (b).

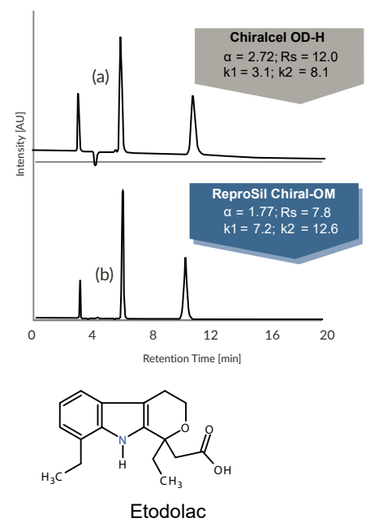


Figure 26: Separation of Etodolac on Chiralcel OD-H (a) and ReproSil Chiral-OM (b).

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Conclusion

ReproSil Chiral-OM is a guaranteed replacement for Chiralcel OD-H columns.

Observation

01.

The selectivity is equivalent either the columns used in basic, neutral or acidic conditions.

02.

Resolution between isomer is higher for ReproSil Chiral-OM column when used in basic & neutral conditions where as in acidic conditions Chiralcel OD-H is showing slightly higher resolution.

03.

The peak symmetry is better for ReproSil Chiral-OM column in all three conditions (i.e. acidic, basic or neutral).

04.

With all the conditions ReproSil Chiral-OM is showing a higher number of theoretical plates.

SFC COLUMNS FOR CHIRAL APPLICATIONS
REPROSIL CHIRAL

Coated ReproSil Chiral Phases from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex

Table 7: Available Coated ReproSil Chiral Phases based on Amylose from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex.

		Particle Size and Part Number (PN)					
Media	**Chiral Selector**	**3 µm**	**5 µm**	**10 µm**	**20 µm**	**Daicel**	**Phenomenex**
ReproSil Chiral-AMS	Amylose tris[((S)-α-methylbenzyl) carbamate]	r63.ams	r65.ams	r60.ams	N/A	Chiralpak AS	N/A
ReproSil Chiral-AM	Amylose tris(3,5-dimethylphenyl-carbamate)	r63.am	r65.am	r60.am	r620.am	Chiralpak AD	Lux Amylose-1
ReproSil Chiral-YM	Amylose tris(5-chloro-2-methylphenyl-carbamate)	r63.ym	r65.ym	N/A	N/A	Chiralpak AY	Lux Amylose-2
ReproSil Chiral-ZA	Amylose tris(3-chloro-4-methylphenyl-carbamate)	r63.za	r65.za	N/A	N/A	Chiralpak AZ	N/A

Table 8: Available Coated ReproSil Chiral Phases based on Cellulose from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex.

		Particle Size and Part Number (PN)					
Media	**Chiral Selector**	**3 µm**	**5 µm**	**10 µm**	**20 µm**	**Daicel**	**Phenomenex**
ReproSil Chiral-BM	Cellulose tris(benzoylcarbamate)	N/A	r65.bm	N/A	N/A	Chiralpak OB	N/A
ReproSil Chiral-JM	Cellulose tris(4-methylbenzoyl-carbamate)	r63.jm	r65.jm	r60.jm	r620.jm	Chiralpak OJ	Lux Cellulose-3
ReproSil Chiral-GM	Cellulose tris(4-methylphenyl-carbamate)	N/A	r65.gm	N/A	N/A	Chiralpak OC	N/A
ReproSil Chiral-OM	Cellulose tris(3,5-dimethylphenyl-carbamate)	r63.om	r65.om	r60.om	r620.om	Chiralpak OD	Lux Cellulose-1
ReproSil Chiral-ZM	Cellulose tris(3-chloro-4-methylphenylcarbamate)	r63.zm	r65.zm	N/A	N/A	Chiralpak OZ	Lux Cellulose-2
ReproSil Chiral-XM	Cellulose tris(4-chloro-3-methylphenylcarbamate)	r63.xm	r65.xm	N/A	N/A	Chiralpak OX	Lux Cellulose-4
ReproSil Chiral-CM	Cellulose tris(phenylcarbamate)	r63.cm	r65.cm	r60.cm	N/A	Chiralpak OC	N/A

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Immobilized ReproSil Chiral Phases

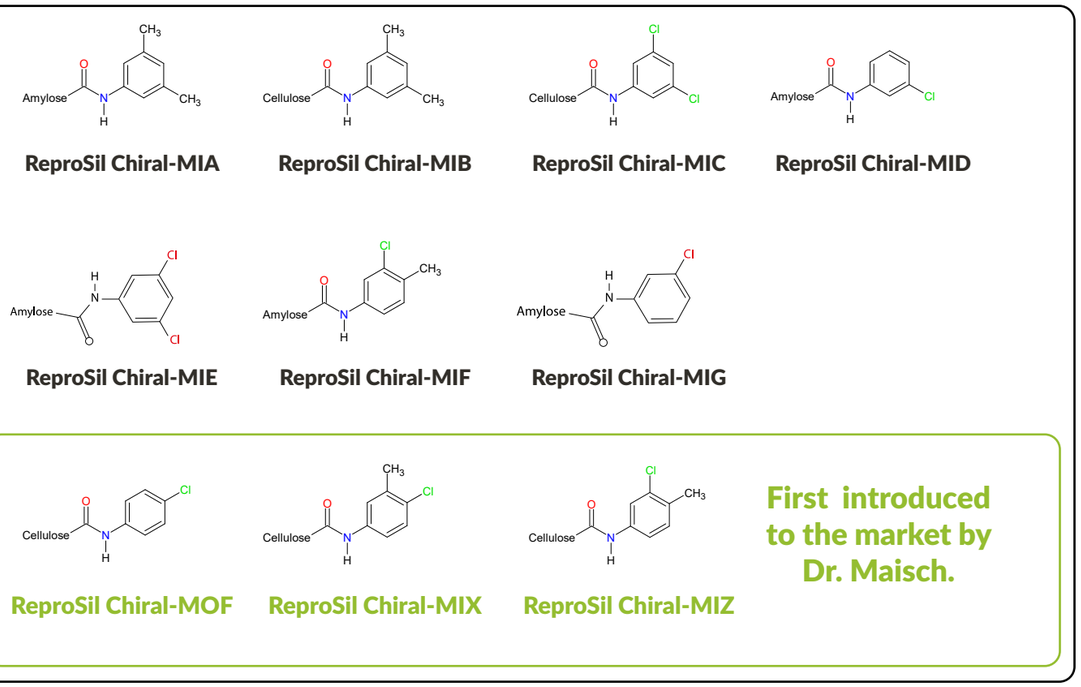

Figure 27: Immobilized ReproSil Chiral Phases from Dr. Maisch.

The immobilized stationary phases ReproSil Chiral-MIA, MIF, MID, MIB, MIC, MIG MIX, MIZ and MOF with greatly increased column robustness tolerate strong organic solvents such as DMSO, DCM, Ethyl Acetate, MtBE and THF to be injected onto the column both as an injection solvent or part of the eluent.

SFC COLUMNS FOR CHIRAL APPLICATIONS
REPROSIL CHIRAL

Immobilized ReproSil Chiral Phases from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex

Table 9: Available Immobilized ReproSil Chiral Phases based on Amylose from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex.

		Particle Size and Part Number (PN)					
Media	**Chiral Selector**	**3 µm**	**5 µm**	**10 µm**	**20 µm**	**Daicel**	**Phenomenex**
ReproSil Chiral-MIA	Amylose tris(3,5-dimethylphenyl-carbamate)	N/A	r65.mia	N/A	r620.mia	Chiralpak IA	Lux i-Amylose-1
ReproSil Chiral-MID	Amylose tris(3-chlorophenyl-carbamate)	N/A	r65.mid	N/A	N/A	Chiralpak ID	N/A
ReproSil Chiral-MIE	Amylose tris(3,5-dichlorophenyl-carbamate)	N/A	r65.mie	N/A	N/A	Chiralpak IE	N/A
ReproSil Chiral-MIF	Amylose tris(3-chloro-4-methylphenylcarbamate)	N/A	r65.mif	N/A	N/A	Chiralpak IF	N/A
ReproSil Chiral-MIG	Amylose tris(3-chloro-5-methylphenylcarbamate)	N/A	r65.mig	N/A	N/A	N/A	N/A

Table 10: Available Immobilized ReproSil Chiral Phases based on Cellulose from Dr. Maisch as Alternatives to Chiral Phases from Daicel and Phenomenex.

		Particle Size and Part Number (PN)					
Media	**Chiral Selector**	**3 µm**	**5 µm**	**10 µm**	**20 µm**	**Daicel**	**Phenomenex**
ReproSil Chiral-MIB	Cellulose tris(3,5-dimethylphenyl-carbamate)	N/A	r65.mib	N/A	N/A	Chiralpak IB	N/A
ReproSil Chiral-MIC	Cellulose tris(3,5-dichlorophenyl-carbamate)	r63.mic	r65.mic	N/A	N/A	Chiralpak IC	Lux i-Cellulose-5
ReproSil Chiral-MIX	Cellulose tris(4-chloro-3-methylphenylcarbamate)	N/A	r65.mix	N/A	N/A	N/A	N/A
ReproSil Chiral-MIZ	Cellulose tris(3-chloro-4-methylphenylcarbamate)	r63.miz	r65.miz	N/A	N/A	N/A	N/A
ReproSil Chiral-MOF	Cellulose tris(4-chlorophenyl-carbamate)	N/A	r65.mof	N/A	N/A	N/A	N/A

Example: Part Number (PN) for ReproSil Chiral-MOF, 5 µm, 250 x 4.6 mm: r65.mof.s2546

NOTE: Other Particle Sizes are available on request.

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Comparison of ReproSil Chiral-OM, ReproSil Chiral-MIX and Lux Cellulose-4

Column:	ReproSil Chiral-OM	**Column:**	Lux Cellulose-4
Particle Size:	5 µm	**Particle Size:**	3 µm
Dimension:	100 x 3.0 mm	**Dimension:**	100 x 4.6 mm
Sample:	Customer Sample		
Mobile Phase:	CO_2/0-20% MeOH (0.1% DEA) in 2 min		

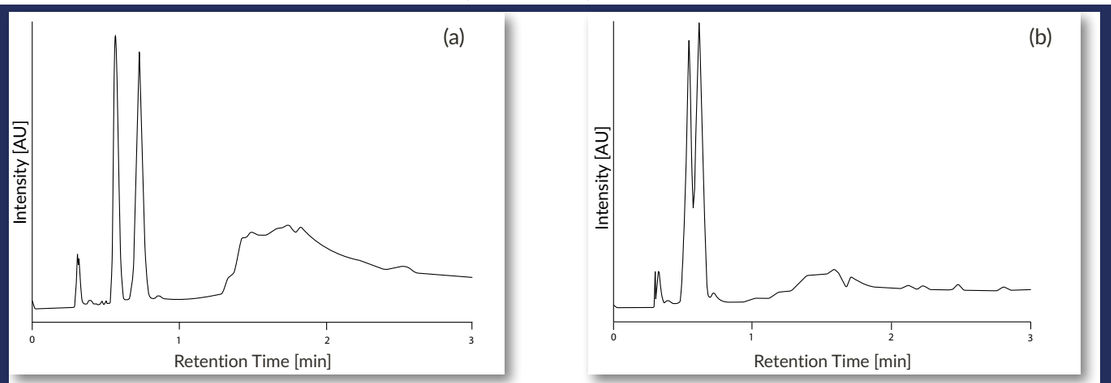

Figure 28: Separation of a Customer Sample on ReproSil Chiral-OM (a) and Lux Cellulose-4 (b).

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	0.564	220320	N/A	1.20
2	0.726	334417	2.26	1.04

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	0.547	647055	N/A	N/A
2	0.626	804384	0.97	N/A

Column:	ReproSil Chiral-MIX	**Column:**	Lux Cellulose-4
Particle Size:	5 µm	**Particle Size:**	3 µm
Dimension:	100 x 3.0 mm	**Dimension:**	100 x 4.6 mm
Sample:	Tetrahydro-2H-1,3-thiazine-2-one (TSO)		
Mobile Phase:	CO_2/10% MeOH (0.1% DEA)		

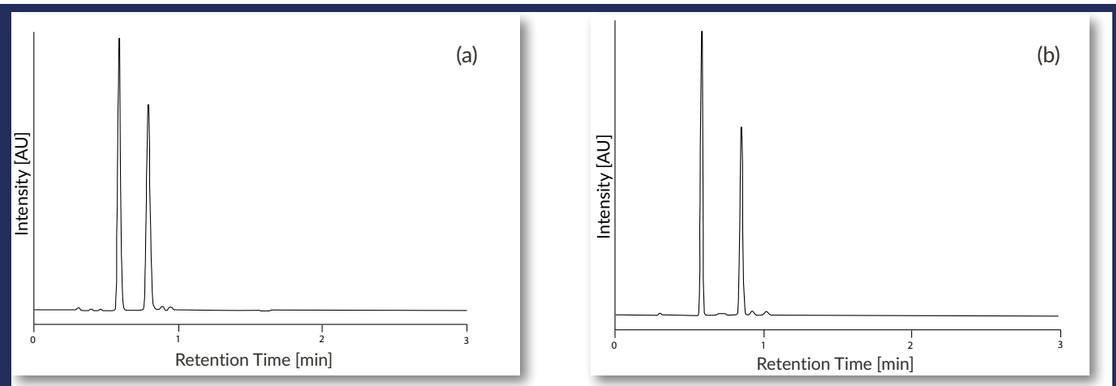

Figure 29: Separation of TSO on ReproSil Chiral-MIX (a) and Lux Cellulose-4 (b).

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	0.588	1970619	N/A	1.13
2	0.789	1999432	4.97	1.11

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	0.583	1038369	N/A	1.05
2	0.851	1041945	8.89	1.04

SFC COLUMNS FOR CHIRAL APPLICATIONS
REPROSIL CHIRAL

Comparison of ReproSil Chiral-MIZ and Lux Cellulose-2

Column:	ReproSil Chiral-MIZ	**Column:**	Lux Cellulose-2
Particle Size:	3 µm	**Particle Size:**	3 µm
Dimension:	100 x 3.0 mm	**Dimension:**	50 x 4.6 mm
Sample:	Customer Sample		
Mobile Phase:	CO_2/10-50% MeOH (0.1% DEA) in 2 min, hold until 5 min		

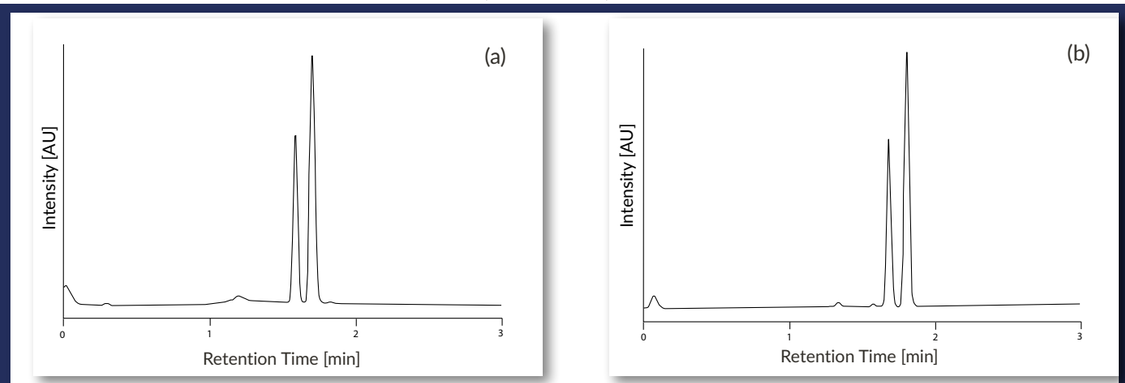

Figure 30: Separation of a Customer Sample on ReproSil Chiral-MIZ (a) and Lux Cellulose-2 (b).

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	1.585	1872263	N/A	1.06
2	1.699	3221889	1.77	1.09

No.	Retention Time [min]	Area [mAU·s]	Resolution	Asymmetry
1	1.678	1757077	N/A	1.05
2	1.801	3005764	2.00	1.06

Immobilized Brush-Type Phase

Immobilized Brush-Type Phase with electron acceptor and donor functionality. Particularly useful for aromatic compounds with O or N near the chiral centre.

This phase shows a very broad versatility and complementary selectivity to ReproSil Chiral Polysaccharide Phases. The Phase is compatible with all commonly used mobile phases, including aqueous systems.

Both antipodes of the chiral selector are available – allowing to reverse the elution order of the enantiomers of a given racemate.

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ReproSil Chiral-NR

ReproSil Chiral-NR showed excellent hit rates in many chiral purification departments of global pharmaceutical companies.

Preparative Chiral Separations Using HPLC – Hoffmann-La Roche, Basel, 2014

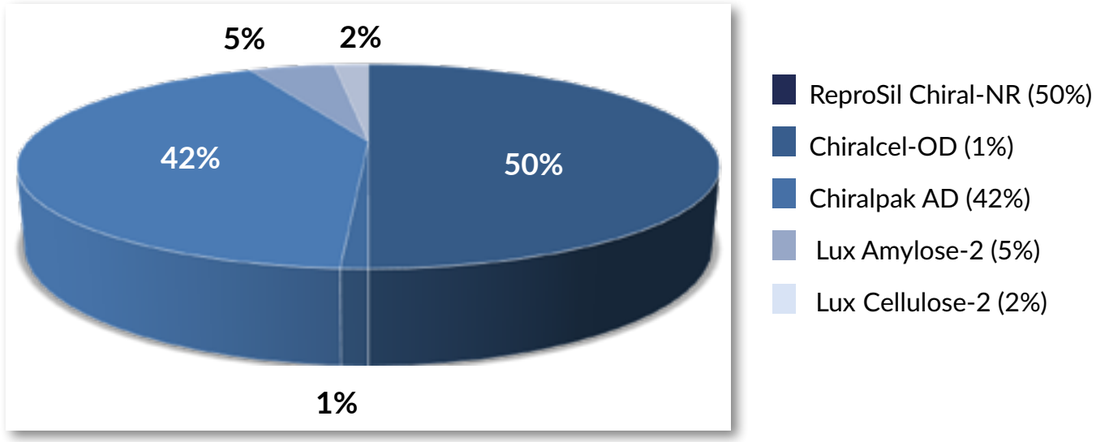

Figure 31: Statistical Evaluation of Chiral SFC Screening of Pharmaceutical Compounds - Hoffmann-La Roche, Basel, 2014.

ReproSil Chiral-NR is available in different Particle Sizes

Table 11: Available Immobilized ReproSil Chiral-NR and ReproSil Chiral-NR-R Media.

		Particle Size and Part Number (PN)			
Media	**Chiral Selector**	**3 µm**	**5 µm**	**8 µm**	**12 µm**
ReproSil Chiral-NR	Immobilized Brush-Type, π-Electron Acceptor / π-Electron Donor	r13.nr	r15.nr	r18.nr	r112.nr
ReproSil Chiral-NR-R [1)]	Immobilized Brush-Type, π-Electron Donor	r13.nrr	r15.nrr	r18.nrr	r112.nrr

1) Inverse Elution Order in comparison to ReproSil Chiral-NR

Example:
Part Number (PN) for ReproSil Chiral-NR, 5 µm, 250 x 4.6 mm: r15.nr.s2546

NOTE:
Other Particle Sizes are available on request.

SFC COLUMNS FOR CHIRAL APPLICATIONS
REPROSIL CHIRAL-NR

Comparison of ReproSil Chiral-NR and Whelk-O 1

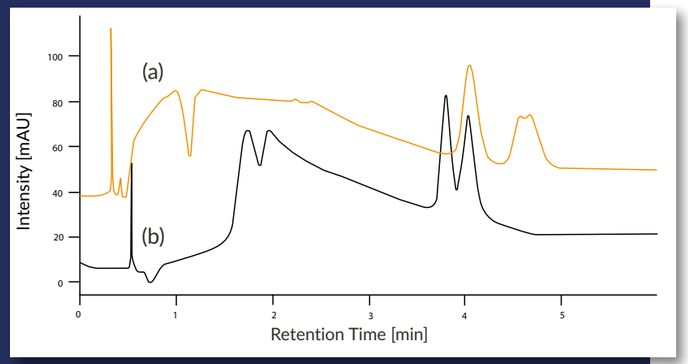

Figure 32: Separation of a chiral Customer Sample on ReproSil Chiral-NR, 8 µm, 100 x 4.6 mm (a) and (R,R)-Whelk-O 1, 5 µm, 150 x 4.6 mm (b).

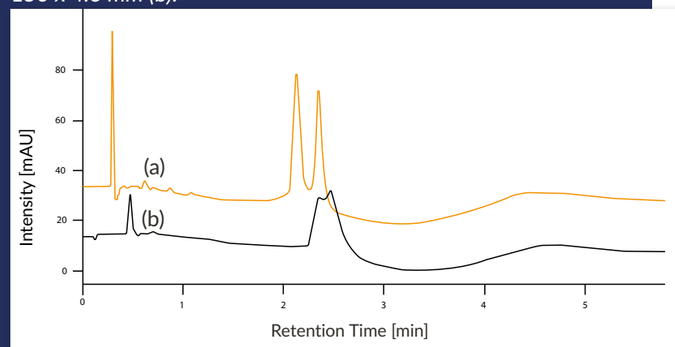

Figure 33: Separation of a chiral Customer Sample on ReproSil Chiral-NR, 8 µm, 100 x 4.6 mm (a) and (R,R)-Whelk-O 1, 5 µm, 150 x 4.6 mm (b).

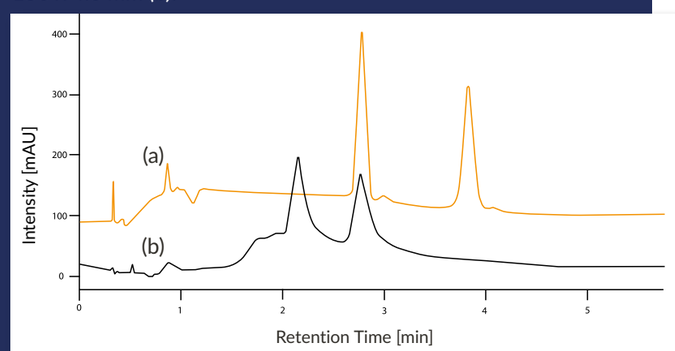

Figure 34: Separation of a chiral Customer Sample on ReproSil Chiral-NR, 8 µm, 100 x 4.6 mm (a) and (R,R)-Whelk-O 1, 5 µm, 150 x 4.6 mm (b).

Column:	ReproSil Chiral-NR, 5 µm
Dimension:	100 x 4.6 mm
Column:	Whelk-O 1, 5µm
Dimension:	150 x 4.6 mm
Mobile Phase:	MeOH + 0.1% DEA
Gradient:	10% - 50% in 2 min hold 1.0 min at 50%
Flow Rate:	4 ml/min
Temperature:	35 °C
Backpressure:	103 bar
Detection:	UV-Detection @220 nm

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SFC Columns for SEC Applications

Polymer analysis can be performed using three modes:

1. Size Exclusion Chromatography (SEC).
2. Liquid Adsorption Chromatography (LAC).
3. Liquid Adsorption Chromatography at Critial Conditions (LACCC).

All three modes can be operated under SFC conditions and offer an excellent approach for PEG analysis on both analytical and preparative scales. Further details can be found in Dr. Maisch's Technical Notification 0007.

Table 12: Available ReproSil SEC Media.

				Particle Size and Part Number (PN)			
Media	**Pore Size [Å]**	**MG-Range [Da]**	**Surface Modification**	**1.9 µm**	**3 µm**	**5 µm**	**10 µm**
ReproSil 50 SEC	50	500 - 10,000	N/A	N/A	N/A	r05.sec	N/A
ReproSil 125 SEC	125	5,000 - 100,000	N/A	N/A	r13.sec	r15.sec	r10.sec
ReproSil 200 SEC	200	10,000 - 500,000	PEG	r219.sec	N/A	r25.sec	N/A
ReproSil 200 SEC-2	200	10,000 - 500,000	DIOL	r219.sec2	r23.sec2	r25.sec2	r20.sec2
ReproSil 300 SEC	300	10,000 - 1,000,000	N/A	N/A	r33.sec	r35.sec	N/A
ReproSil 4000 SEC	600	20,000 - 500,000	N/A	N/A	N/A	r45.sec	N/A
ReproSil 5000 SEC	800	150,000 - 1,250,000	N/A	N/A	N/A	r55.sec	N/A

PREPARATIVE SFC COLUMNS

SFC is particularly attractive on a preparative scale, as the CO_2 in the mobile phase can be easily removed during depressurization and potentially recycled. Only a small amount of co-solvent is left. The time savings represent a significant advantage over Normal-Phase (NP) or Reversed-Phase (RP) preparative purifications.

Dr. Maisch offers all Dr. Maisch Media in prep-column dimensions.

The superior hardware type for prep columns is the LONGLIFE Hardware.

Benefits of the LONGLIFE Hardware:

- Packed by Piston.
- Flexible Bed Length.
- Static Axial Compression (SAC) Mechanism.
- Packing and Repacking Service.
- Available ID: 25, 30, 40, 50, 70 mm.
- Scalability to > 150 mm ID - Using MODcol columns in combination with the MODcol Multipacker Instruments.

The LONGLIFE Hardware even allows to pack 3 µm particles in prep dimension which results in an extremely high efficiency.

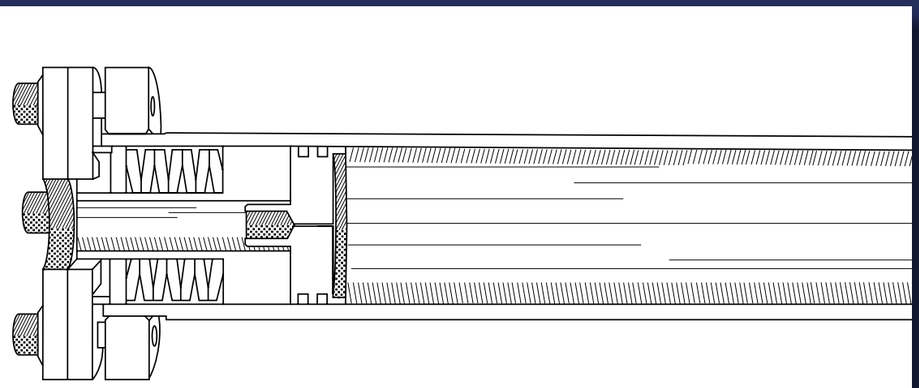
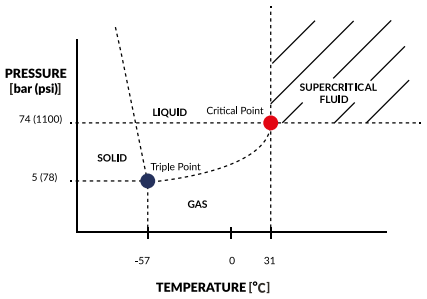


Figure 34: Longlife Hardware.

Dr. Maisch

Any Column, Any Size, Any Media

Distributor:



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