Boost your productivity, lower your costs

Kromasil®

The way to peak performance in liquid chromatography

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Why the best silica costs the least

Kromasil's business idea since its introduction in 1988 is to offer you the lowest possible total separation cost by providing the highest quality silica-based HPLC, SMB and SFC packing material available. The superior loadability and lifetime mean you can reduce the cost for solvent and other parts, and increase productivity. The packing material is at the heart, and the single most important factor that determines the performance of your processes.

HIGH AVAILABLE SURFACE AREA ▶ HIGH LOADABILITY ▶

IMPROVED PRODUCTIVITY/REDUCED COSTS

EXCELLENT MECHANICAL AND CHEMICAL STABILITY ▶ LONG LIFETIME ▶

IMPROVED PRODUCTIVITY/REDUCED COSTS

You'll be amazed at how much it can take

High loading capacity is key to high productivity and the best total economy in your industrial scale HPLC, SMB or SFC. A high available surface area for your target molecule, together with an optimized surface chemistry to maximize the separation factor, will result in high productivity and low production costs.

THE KROMASIL PARADOX

A high surface area can be obtained by increasing the pore volume. However, this will normally result in a very weak material, with low mechanical strength.

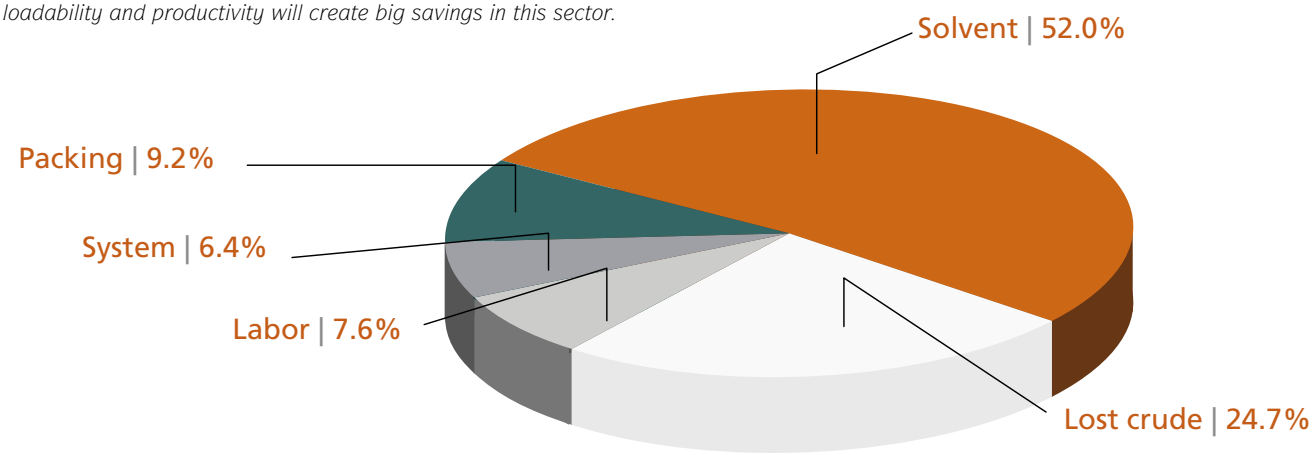
Kromasil combines a high pore volume, resulting in a high surface area, with extremely high mechanical strength. This is unique among silica-based packing materials.

In addition, the pore size distribution is very small, resulting in a high available surface area. For every application you have, there is an optimal pore size that will maximize the loading capacity.

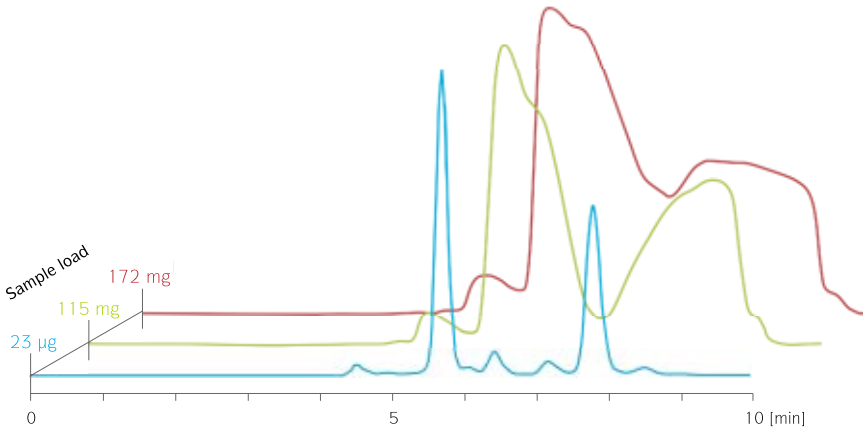
SURFACE CHEMISTRY AND SELECTIVITY

In Reversed Phase HPLC, the type and density of the ligands will determine how much you can load onto the column. Kromasil's well-defined chemistry, with a high density of adsorption sites, ensures that the peaks will remain narrow even under high loading. At the end of the day, this is what gives you a cost-effective HPLC process.

The figure shows a real life separation of a chiral compound, with a typical cost distribution between solvent, lost crude, labor, system and packing cost. The solvent normally dominates, making up 50–80% of the total cost. An increase in loadability and productivity will create big savings in this sector.



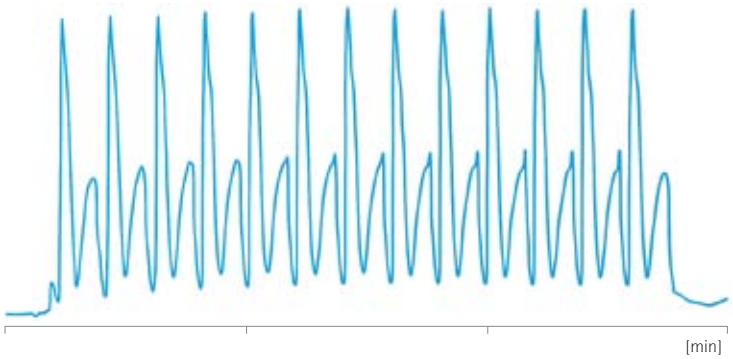
Preparative injections of Oxirane on Kromasil CN



Conditions
Stationary phase: Kromasil CN, 60 Å, 10 µm
Column size: 4.6 x 250 mm
Solute: Oxirane
Flow rate: 1.16 ml/min
α = 1.8
k'_1 = 0.9

Kromasil Cyano was used for the large-scale separation of a diastereomeric oxirane, where the chromatograms show the scale-up experiments in analytical scale. Even at a loading corresponding to 172 mg loading in analytical scale, i.e. 86 mg crude/g of packing, 98–99% pure diastereomers could be obtained in the two collected fractions. Recovery was close to 100%.

Stacked injections of Oxirane on Kromasil CN



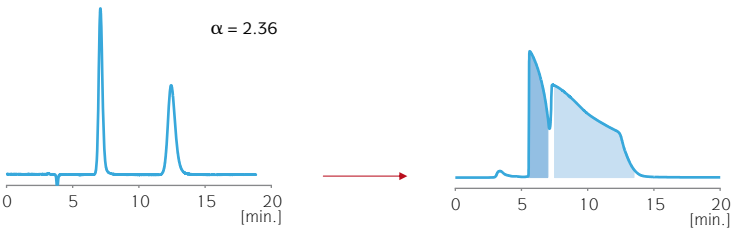
Conditions
Stationary phase: Kromasil CN, 60 Å, 10 µm
Column size: 4.6 x 250 mm
Solute: Oxirane
Temperature: 25°C
Flow rate: 2.0 ml/min.
Loading: 172 mg (crude)/2.6 min
Productivity: 2.0 kg/(h·kg packing)

In order to maximize productivity a stacked injection technique was applied, where cycle time between injections is only 2.6 minutes. For a 200 mm ID column, 180 kg of crude can be purified per day using this method.

Preparative injection of Metoprolol on Kromasil CelluCoat

Analytical injection
Sample size: 10 µg
Detection: UV 223 nm

Preparative injection
Sample size: 20 mg
Detection: UV 290 nm



	Enantiomer 1	Enantiomer 2
Purity [%]	100	99.7
Yield [%]	97.9	88.1

Conditions
Stationary phase: Kromasil CelluCoat, 10 µm
Column size: 4.6 x 250 mm
Temperature: 25°C
Flow rate: 1 ml/min
Solute: Metoprolol
Mobile phase: Heptane / 2-Propanol / DEA (90/10/0.1)
Loading capacity: 9.6 mg/g (packing)

The chromatograms show a chiral scale-up example on Kromasil CelluCoat. The loading capacity lies close to the capacity for a regular achiral RP phase.

Strong enough to save your budget

In modern HPLC, SMB and SFC systems, small efficient particles are used for the best total economy. At the same time, it's also common with large diameter dynamic axial compression columns, which results in very high mechanical stress on the particles. To ensure a problem-free process, with no breakdown of the particles, high mechanical strength is crucial.

WHY HIGH MECHANICAL STRENGTH?

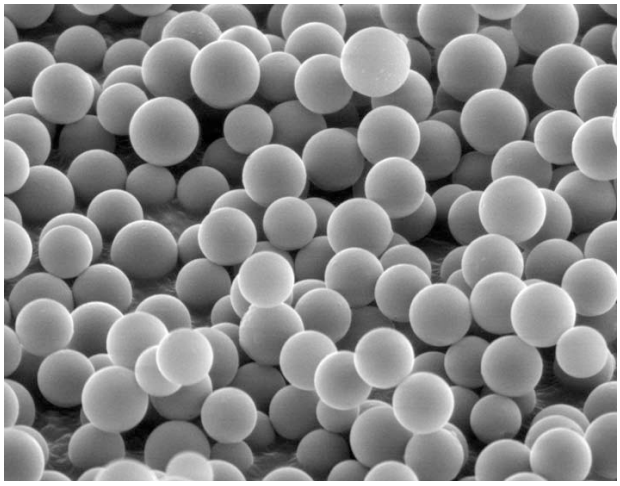
The primary reason is to withstand mechanical stress in the column. A silica packing is also often exposed to high mechanical stress when unpacked and packed again in production.

Frequent packing and unpacking requires a very stable packing material where no fines creation can be tolerated. If fines are formed in any part of the process this will result in an increasing back-pressure. Eventually the pressure limit for the system is reached, and the column has to be repacked with new material.

THE FACTORS BEHIND A STABLE MATERIAL

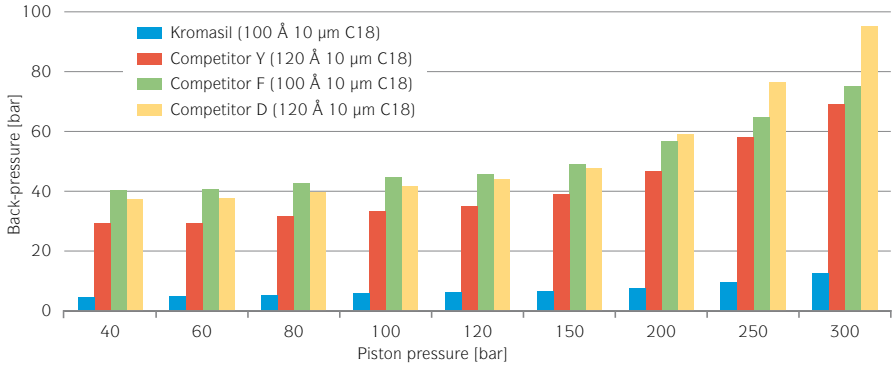
The Kromasil particles are essentially perfectly spherical. In addition, the pore shape and structure is more regular than other materials. The result is mechanical strength that allows extremely high piston pressure in your column.

Many Kromasil customers perform Cleaning In Place (CIP) using highly alkaline conditions to remove adsorbed polypeptide impurities, especially in insulin purification. Such conditions will quickly break down less stable materials mechanically. But with Kromasil, you can apply CIP over and over again.



The Kromasil particles are almost perfectly spherical, which is part of the explanation for very high mechanical stability.

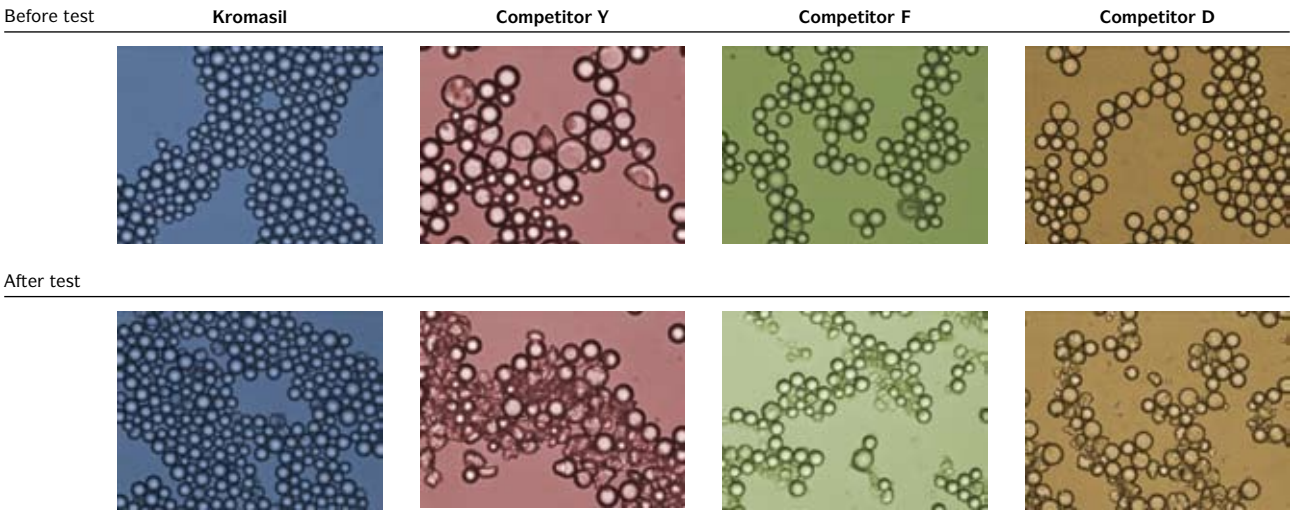
Pressure over packed bed during 2nd cycle of mechanical stability test



Test conditions
The test material is packed in a 50 mm ID DAC column, and the pressure is increased step-wise, from 40 bar up to 300 bar. The back-pressure is monitored during the process using ethanol as the mobile phase. The test material is unpacked from the column after the first cycle, re-slurried, packed again, and a second test cycle is applied. The resulting back-pressure during the second cycle is shown in the diagram.

To simulate a repeated packing procedure without emptying the column, a test method with a successive increase of piston pressure was developed. The relative back-pressure increase is a measure of the degree of degradation of the material after repeated packings.

Light microscope pictures showing the appearance of the particles before and after the stability test



Stable even when the going gets tough

A purification process of a pharmaceutical or a biopolymer can consist of steps at very low or very high pH—for the chromatography and for the cleaning procedure. This puts very high demands on the chemical stability of the packing material, both for the bonded phase and the silica matrix itself.

THE SECRET OF THE BONDED PHASE

At low pH the bonded phase can be hydrolyzed, resulting in a less hydrophobic surface and reduced retention times for lipophilic compounds. Kromasil's high ligand coating density, with an efficient end-capping, will ensure a low degree of hydrolysis.

For high pH conditions, Kromasil's extensive coating will ensure that the alkaline mobile phase to a large extent will be kept away from the silica surface.

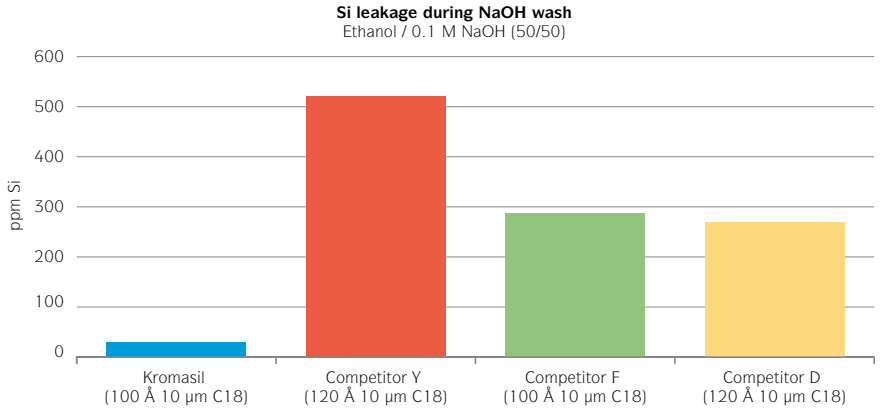
A STABLE SILICA MATRIX

The Kromasil silica matrix is produced using a sol-gel technology, resulting in a very regular structure. After the gelling, the particles are subjected to several further steps to improve both the chemical and mechanical stability. The result is a superior silica matrix. So even if the silica surface is attacked by an alkaline mobile phase, the matrix itself will be extremely resistant.

All in all, the result is the long lifetime of Kromasil packing material.

Chemical stability: Crucial for the lifetime of the packing and for a problem-free process.

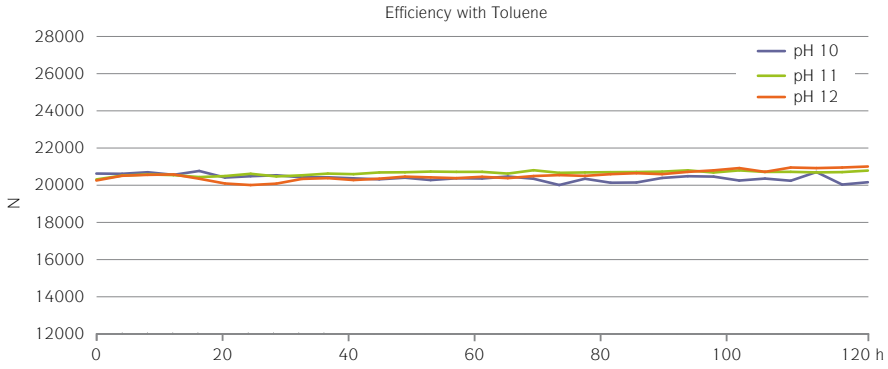
Chemical stability under alkaline conditions



Conditions
Mobile phase: Ethanol / Water, 0.1 M NaOH, pH13 (50/50)
Flow rate: 1.0 ml/min, for 10 column volumes (contact time: 41.5 min)
Temperature: 20°C

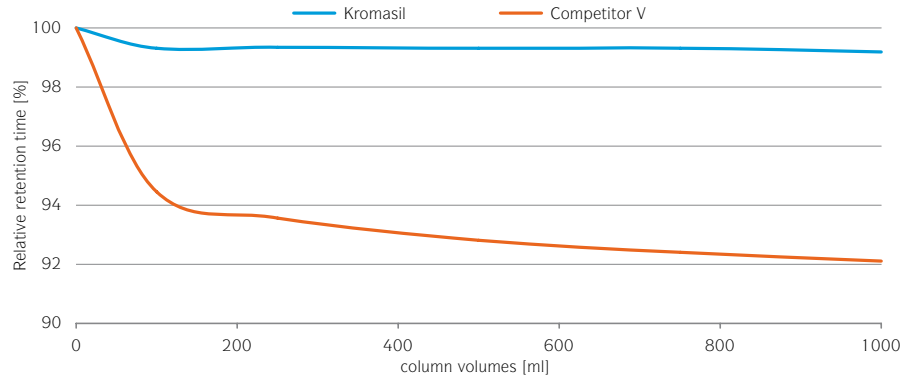
To remove adsorbed polypeptide impurities, especially in insulin purification, a high pH CIP (Cleaning In Place) step is often applied. The figure shows the leakage of silicon under conditions that simulate the situation during insulin production.

Long-term chemical stability of Kromasil 100 Å C18 under alkaline conditions



Conditions
Stationary phase: Kromasil 100 Å C18
Column size: 4.6 × 250 mm
Mobile phase: Acetonitrile / buffer (50/50)
Buffers: 50 mM Trimethylamine / Acetate at pH 10.0, pH 11.0 and pH 12.0, respectively.
Flow rate: 1.0 ml/min during analysis
0.1 ml/min between analyses
Temperature: 25°C
Detection: UV 254 nm

Long-term chemical stability at low pH



Conditions
Stationary phase: Kromasil 300 Å C4
Column size: 4.6 × 250 mm
Mobile phase: Acetonitrile / Water / TFA (50/50/1)
Flow rate: 2 ml/min
Temperature: 20°C

Long-term chemical stability is key to the long lifetime of packing material. The adjoining figures show the situation at both high and low pH, giving a good indication of the longevity of Kromasil.

Easy to scale up, easy to track down

The beauty of Kromasil is that you always get the same high performance regardless of column size. Our manufacturing starts with the silica raw material, and runs all the way through to the finished silica-based packing material. We produce very large batches, so whatever your demand is, we can supply. And quality will be the same, over and over again.

WITH YOU ALL THE WAY …

With Kromasil you always experience the same high performance, regardless of column size. The secret is that we produce a large silica batch and then fractionate it. This way, we can offer the entire range of available particle sizes in any amount.

Whether you choose to purchase a small column, or hundreds of kilos for large-scale production, the silica will come from the same batch. This means that properties such as particle size distribution, selectivity and loadability are identical, making it easy to scale up.

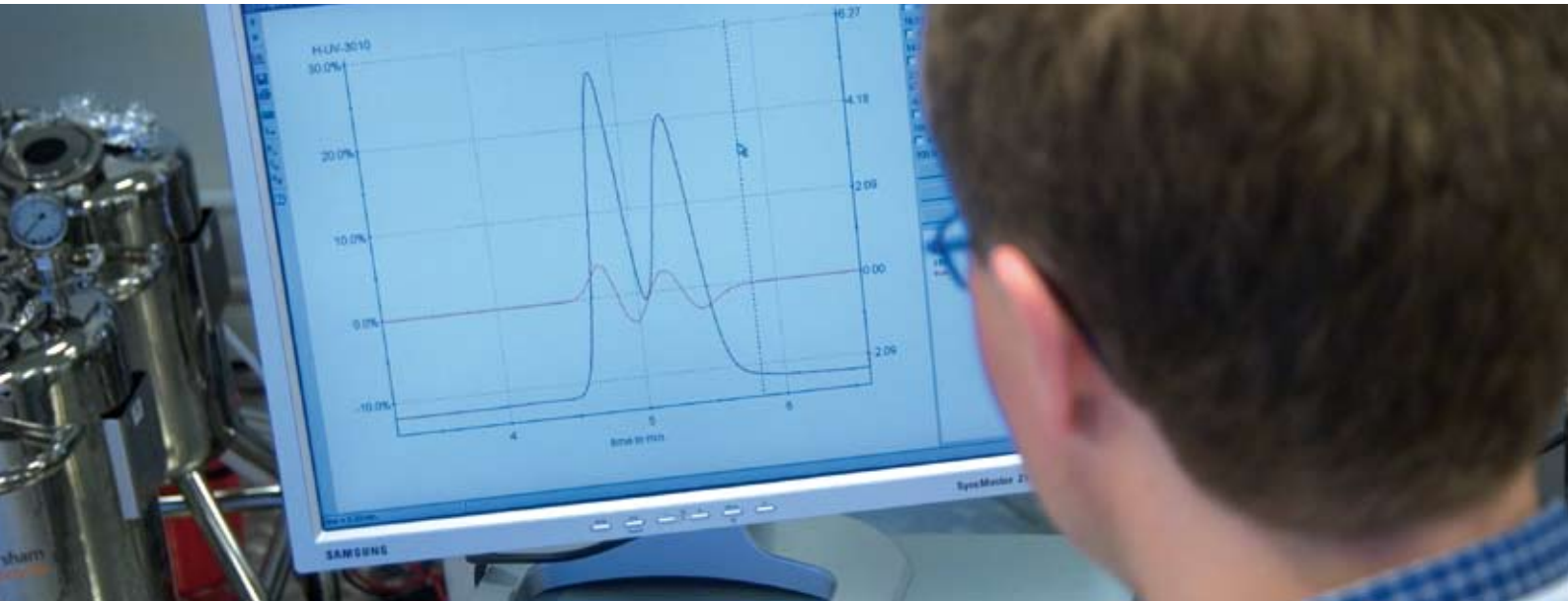
… AND BACK AGAIN

Kromasil is back-integrated from the silica raw material to the finished bonded silica-based packing material. Less than a handful of suppliers worldwide control the entire manufacturing process as well as Kromasil, or come even close to the multi-ton per year production capacity of Kromasil.

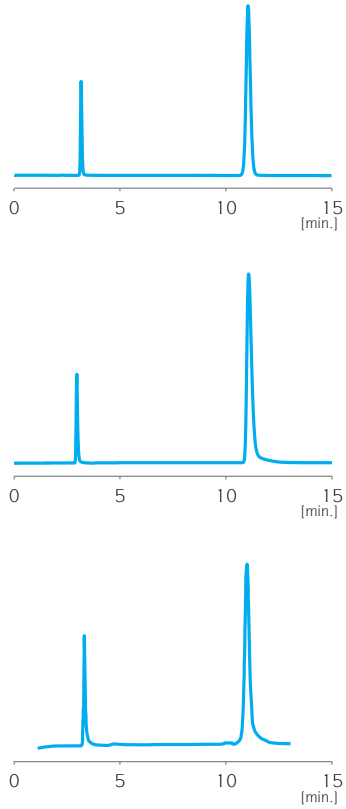
HIGH QUALITY PRODUCTS DELIVERED IN TIME

Reproducibility between batches is very important in production, where a variation in the properties of the silica could mean the loss of millions of dollars. Since we control the total manufacturing process we can easily guarantee the highest quality of the final product. Kromasil has been ISO 9001 certified since the early nineties.

We can also offer high delivery precision, with batch sizes exceeding 300 kg per batch, and multi-ton per year production. In addition, you get access to over 60 years of experience in silica technology.



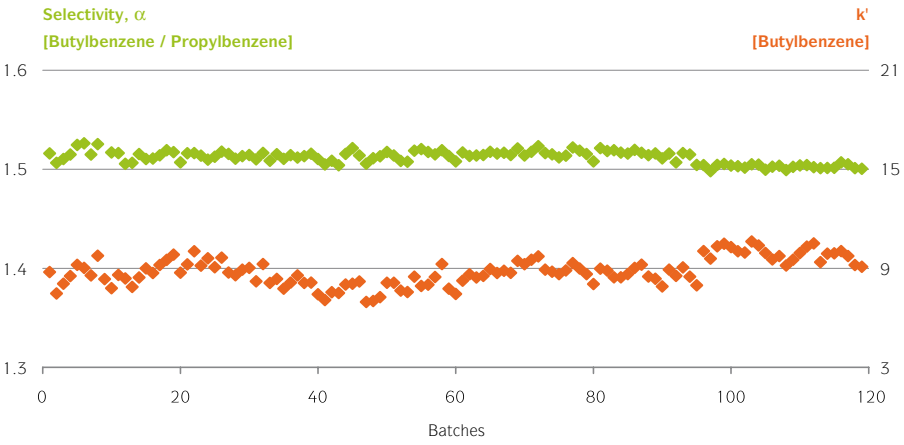
Scalability—the same high performance in any column size



Common conditions
Stationary phase: Kromasil 100 Å C18, 10 µm
Sample mix: Uracil and Toluene
Mobile phase: Acetonitrile / Water (30/70)
Detection: UV 254 nm
Column length: 250 mm
Linear velocity: 0.66 mm/s

All Kromasil pre-packed columns are delivered with a minimum performance guarantee of at least 40 000 pl/m for 10 µm particles. For larger diameters DAC columns are recommended. The performance obtained in analytical columns can be maintained all the way up to very large industrial scale DAC columns, and in the example an 80 cm ID DAC column is proven to show analytical performance. The scale-up factor from the analytical column in this case is 30 000 times!

Batch to batch reproducibility of 120 batches of Kromasil 100 Å C18



Conditions
Stationary phase: Kromasil 100 Å C18
Column size: 4.6 × 250 mm
Sample mix: Butylbenzene and Propylbenzene
Mobile phase: Acetonitrile / Water (30/70)
Flow rate: 2.0 ml/min
Detection: UV 254 nm

In the quality assurance and control of Kromasil, a vast number of tests are performed. In the adjoining figure, batch to batch reproducibility of Kromasil, measured as selectivity and retention factor over time, is shown for particle sizes from 7 µm to 16 µm.

Who could give you better answers than the market leader?

Unlike most other companies in the field of packing material for large scale HPLC, SMB and SFC, Kromasil not only supplies the packing material itself, but is also a leader in the field of developing and optimizing methods for the separation. Our team can advise on how to pack columns, select optimal running conditions or optimize large-scale purifications.

TECHNICAL SUPPORT FROM THE TECHNOLOGY LEADER

The Kromasil team has accumulated a wealth of know-how over the years, and is always on hand to help you with questions or problems that arise. With broad experience of separating complex substances around the world, our chemists and chemical engineers can usually pinpoint any problem simply through a dialog with the customer.

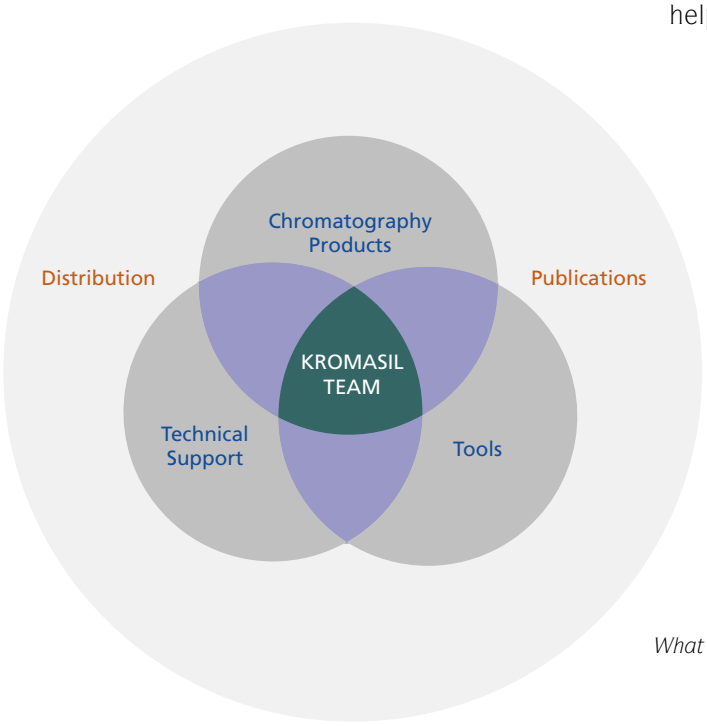
Our applications group can also perform a method development for your application, and optimize the running parameters to give you the most economical separation process possible. This can be done with KromaGuide, a computerized simulation tool that helps optimize your separation to give the most economical running conditions.

In addition, an extensive application guide indicating suitable conditions is available.

A GLOBAL NETWORK FOR SUPPORT

Kromasil has a global network of dedicated distributors for pre-packed columns and smaller amounts of bulk packings. To find your nearest distributor, please see our website or contact us directly.

For larger quantities of Kromasil, our sales offices in Sweden, USA, China and India will gladly help you.



What you get from us

Everything you need, everywhere

Applications for large-scale HPLC comprise everything from small, synthetic pharmaceuticals up to large polypeptides or proteins. In addition, the demands for purity and recovery are constantly increasing. Kromasil has superior packings for the entire range to meet all your needs.

INDUSTRIAL SCALE HPLC TODAY

Industrial scale HPLC is used for synthetic or semi-synthetic small drugs, peptides, and proteins. The biggest application worldwide is insulin, being produced in very large volumes. A growing application is chiral separations, where the demands for pure enantiomers have increased.

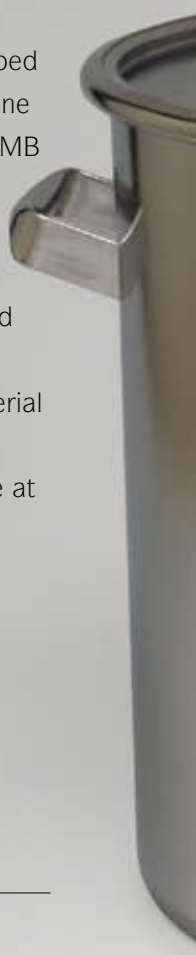
THE KROMASIL PRODUCT PORTFOLIO

The availability table below summarizes the standard Kromasil products available. Phases go from bare silica and polar ligands for normal phase HPLC, to non-polar phases for reversed phase conditions. Pore sizes comprise 60 Å, 100 Å, and 300 Å, to be suitable for everything from small molecules up to proteins.

For our coated polysaccharide chiral phases, CelluCoat™ and AmyCoat™, an in-house developed super wide-pore silica is used. There is also a line of covalently bonded chiral phases available, DMB and TBB, based on 100 Å Kromasil silica.

HOW TO ORDER KROMASIL

To order Kromasil bulk material, we recommend that you contact us directly. Our distributors specialize in columns, but will handle bulk material up to 2 kg quantities. For contact information, please see this brochure or consult our website at www.kromasil.com



Availability of Kromasil

Kromasil 60 Å bulk packings

Phases	Particle sizes, µm 5	7	10	13	16
SIL	■	■	■	■	■
CN	▪	□	■	□	■
Diol	▪	□	■	□	□

Kromasil 100 Å bulk packings

Phases	Particle sizes, µm 3.5	5	7	10	13	16
SIL	■	■	■	■	■	■
C4	▪	▪	■	■	■	■
C8	▪	▪	■	■	■	■
C18	▪	▪	■	■	■	■
NH2	▪	▪	■	■	■	■
Phenyl	□	▪	□	■	□	■

Kromasil 300 Å bulk packings

Phases	Particle sizes, µm 5	10	16
SIL	■	■	■
C4	▪	■	■
C8	▪	■	■
C18	▪	■	■

Kromasil Chiral bulk packings

Phases	Particle sizes, µm 3	5	10	16	25
DMB	□	▪	■	■	□
TBB	□	▪	■	■	□
AmyCoat	▪	▪	■	□	■
CelluCoat	▪	▪	■	□	■

■ = Available as standard product ▪ = Only available in pre-packed Kromasil columns □ = Not available as standard product


Kromasil C8

The moment you adopt our Kromasil High Performance Concept, you join thousands of chromatographers who share a common goal: to achieve better separations when analyzing or isolating pharmaceuticals or other substances.

Not only will you benefit from our patented silica technology, but you gain a strong partner with a reliable track record in the field of silica products. For the past 60 years, Eka Chemicals has pioneered new types of silica. Our long experience in the field of silica chemistry is the secret behind the development of Kromasil, and the success of our Separation Products Group.

Kromasil is available in bulk, or in high-pressure slurry-packed columns.

The development, production and marketing of Kromasil are ISO 9001 certified.

Eka Chemicals is a global company with 2 900 people and production in 18 countries. It is a business unit within AkzoNobel, one of the world's largest chemical groups, with more than 60 000 employees in 80 countries.

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