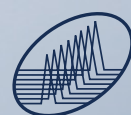




SEPARATION IS OUR **STRENGTH**

SEPBOX AND SEPMATIX



sepiatec
SEPARATION | INNOVATION | AUTOMATION



SEPBOX SYSTEMS

Automated purification of compounds from natural sources

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SEPMATIX SYSTEMS

8x parallel HPLC for screening applications

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INTRODUCTION TO SEPBOX SYSTEMS

Nature has a practically infinite variety of useful compounds ...

Throughout history, valuable therapeutic ingredients have always been derived from plants. One well-known example is the willow tree, whose bark was used by the famous Greek physician Hippocrates to treat inflammatory diseases around 400 B.C. The effective natural ingredient extracted from this bark has been developed by scientists to make Acetylic Acid, which forms the basis of many current pain relievers. Today, we use a substance extracted from a nut tree in the Philippines to treat epilepsy. And Curare, a neurotoxic substance derived from lianas vines in the Amazon jungle, is used to relax muscles and treat tetanus.

Natural compounds still play an increasingly important role in many areas of research and development. Their structural diversity is enhanced by the synthetic potential of combinatorial chemistry. There are many new classes of substances waiting to be

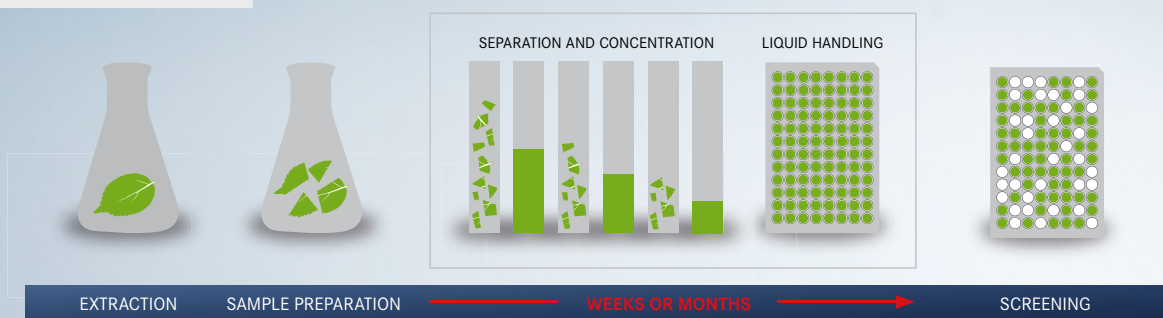
discovered, and the diversity of these compounds and their chiral properties means that some of these are certain to be highly marketable. Pharmaceutical research is only just beginning to exploit this diversity.

... unfortunately, they are never found in their pure state

Access to nature's inexhaustible supply of compounds has increased over recent years. However, unfortunately there isn't the same limitless supply of ways to process them automatically. Fractionation and separation of samples obtained from nature remain time-consuming, tedious and extremely expensive, even though the assays for testing these samples have become faster and more cost-effective thanks to advanced high-throughput screening processes.

Today, High Performance Liquid Chromatography (HPLC) is the standard technology used for separating compounds from natural resources.

Conventional method



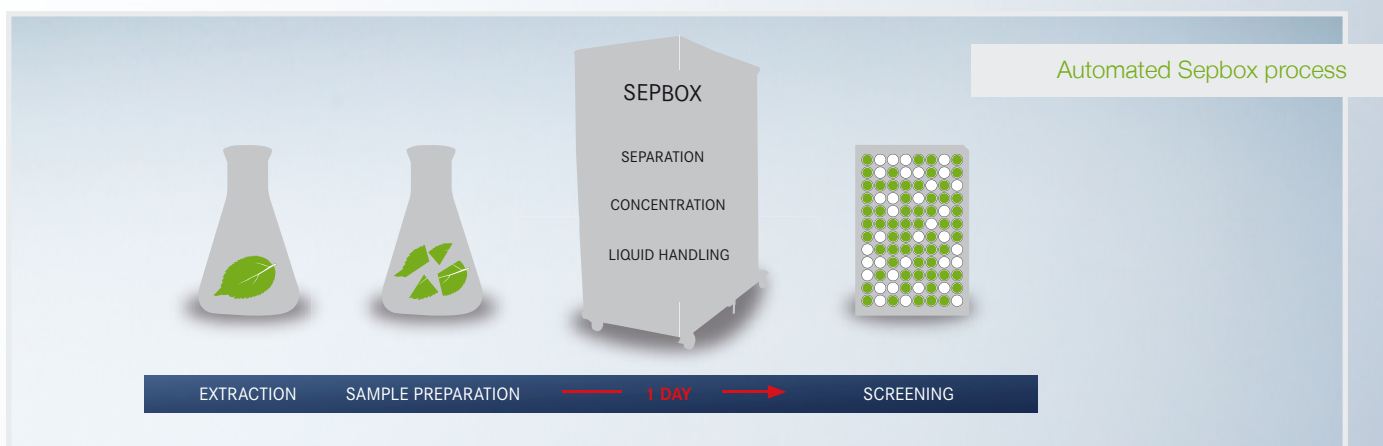
That's why we need state-of-the-art solutions ...

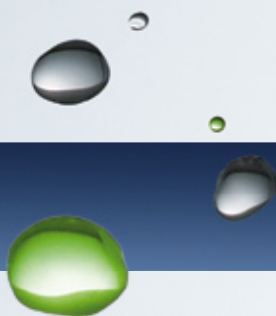
Processing natural product extracts represents a major bottleneck that is constricting the pace of drug discovery. To ensure that sample preparation is both reproducible and reliable, it would therefore be of immense benefit to have an automated process in place for natural compound purification. The economic potential of this is tremendous.

... like Sepbox systems

Sepiatec's unique Sepbox systems allow samples to be processed automatically, and significantly accelerate the purification process. Results which usually take weeks or months with conventional methods can be obtained in just a few days – or even one day – with a Sepbox system.

The Sepbox concept is based on a patented combination of High Performance Liquid Chromatography (HPLC) and Solid Phase Extraction (SPE) – reliable and proven techniques that provide a universal platform suitable for processing large sample numbers. Up to 600 fractions with a very high yield of pure compounds can be efficiently obtained from subsequent High Throughput Screening. Using two-dimensional separation, the recovery rate for both polar and non-polar substances is usually above 90 per cent. Using an automated and highly reproducible process, one extract can be completely separated per day. The pure individual components are soluted in suitable solvents and can be collected in microtiter plates or vials.





SEPBOX 2D-250

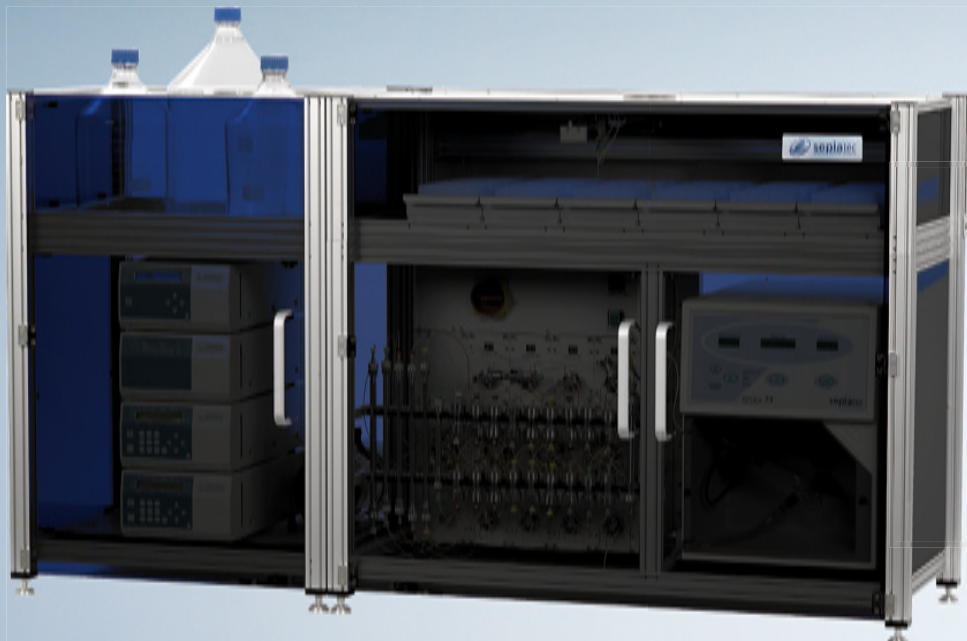
Extensive lab facilities are no longer essential to separate a large number of novel compounds.

With a Sepbox system, up to 600 fractions can be produced per day, many of them containing pure compounds, without investing large amounts in human resources or research facilities. This saves time and money and significantly accelerates the early stages of the product development process.

The automated Sepbox 2D-250 and 2D-5000 systems allow extracts from plants, marine organisms, microbiological or animal

materials to be processed in quantities of up to 250 or 5,000 milligrams respectively. If required, highly polar substances can be separated using the Polar Setup. The systems are equipped with two detectors: UV detection (ultraviolet) and optional ELSD detection (evaporative light scattering detection), which can detect almost all substances.

The **Sepbox 2D-250** benchtop model is designed for the automated two-dimensional separation of up to 250 milligrams of extracts. The system offers the choice between liquid and adsorbed (solid) sample injection. Up to 600 fractions can be collected in microtiter plates in just 24 hours. Depending on the extract, up to 30 per cent of all fractions usually contain pure compounds.

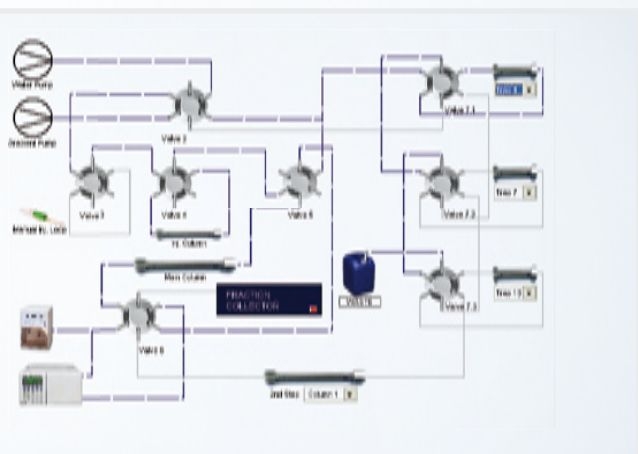


SPECIFICATIONS

Modes of operation	Medium to non-polar, Polar Setup (optional)
Sample size	Max. 250 mg of extract
Pumps	2 HPLC pumps
Columns	1 injection column, 1 main separation column, 3 second separation step columns (6 with Polar Setup), 18 trap columns
Detection	UV detector, ELSD detector (optional)
Fraction collection	FractionCollector with micro-titer plates, 24 deep-well, 48 or 96 well plates
Modes of collection	Time and peak based
Valves	13 electrically actuated valves
Software	Sepbox Control Software
Dimensions	170 x 60 x 75 cm (W x D x H)
Weight	150 kg including FractionCollector

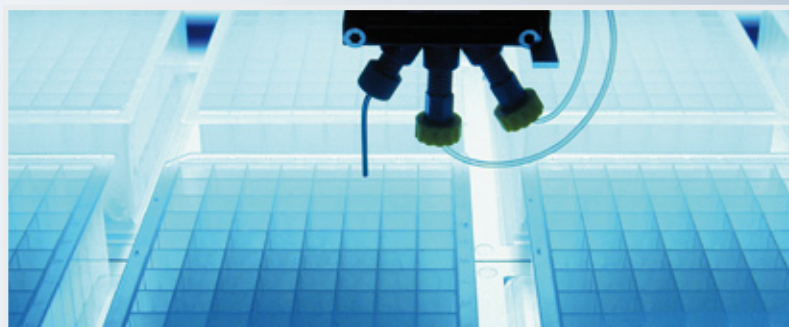
The Sepbox 250 is suitable for medium to non-polar compounds (Polar Setup optional).

The system is equipped with intuitive, **user-friendly software** for method development, process control, data acquisition and data analysis.



ORDER INFORMATION

Art. No.	Device
150-01	Sepbox 2D-250 For medium to non-polar compounds
150-02	Sepbox 2D-250 with ELSD For medium to non-polar compounds
150-03	Sepbox 2D-250 with Polar Setup For polar to non-polar compounds
150-04	Sepbox 2D-250 with ELSD and Polar Setup For polar to non-polar compounds
150-05	Sepbox 2D-250 Polar Setup upgrade





SEPBOX 2D-5000

Sepbox 2D technology has even more to offer. The Sepbox 2D-5000 is designed for a larger workload of up to 5,000 milligrams of extract from natural sources. The automated 2D chromatography provides up to 576 fractions in 24 hours. The FractionCollector is equipped with six removable racks, each containing 96 vials with a maximum capacity of 45 millilitres.

The Sepbox 2D-5000 is also equipped with software for method development, process control, data acquisition and data analysis. On average, up to 30 per cent of all fractions contain pure compounds depending on the extract. The fractions are almost free of water and buffer from the second SPE step and can be processed immediately. Optional Polar Setup is available for polar substances.

The Sepbox 2D-5000 system provides many individual chemical entities in quantities which can be easily used to elucidate structures, screen different targets and build a diverse library.



SPECIFICATIONS

Modes of operation	Medium to non-polar, Polar Setup (optional)
Sample size	Max. 5,000 mg of extract
Pumps	4 preparative HPLC pumps
Columns	1 injection column, 1 main separation column, 3 second separation columns (6 with Polar Setup), 28 trap columns
Detection	2 UV detectors, 1 ELSD detector
Fraction collection	FractionCollector with 6 racks, 96 vials each, max. capacity 45 ml/vial, max. 576 fractions
Modes of collection	Time and peak based, baseline collect (optional)
Valves	67 pneumatically actuated valves
Software	Sepbox Control Software
Dimensions	Sepbox 170 x 94 x 193 cm (W x D x H) FractionCollector 140 x 76 x 168 cm (W x D x H)
Weight	Sepbox 800 kg, FractionCollector 210 kg



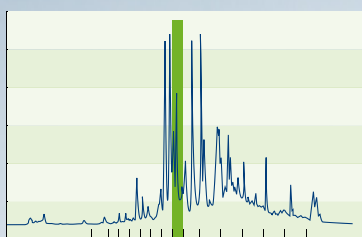
ORDER INFORMATION

Art. No.	Device
100-01	Sepbox 2D-5000 For medium to non-polar compounds
100-02	Sepbox 2D-5000 with Polar Setup For polar to non-polar compounds
100-03	Sepbox 2D-5000 Polar Setup upgrade

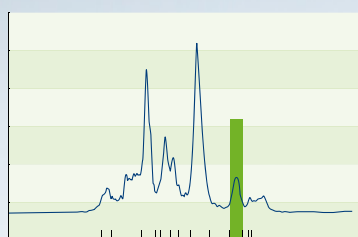


PURITY OF SEPBOX FRACTIONS

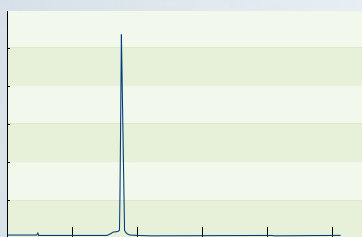
1. Sepbox: first-dimension separation



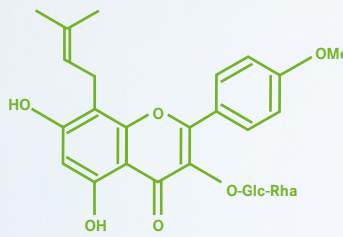
2. Sepbox: second-dimension separation



3. Analytical HPLC examination



4. Structure elucidation

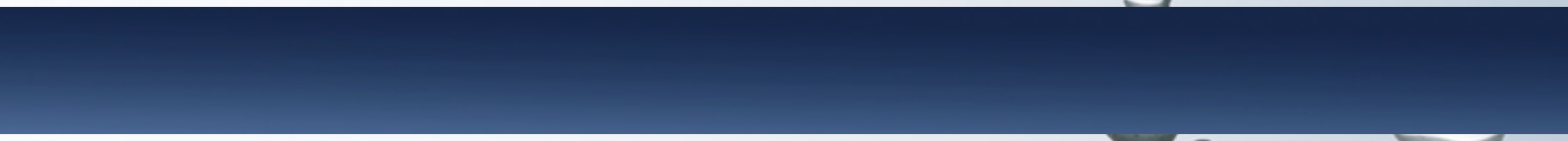


The benefit of using a two-dimensional Sepbox system is clear: not only does the system separate an extract from natural resources into about 600 fractions within 24 hours, but many of these fractions contain single components with a purity level of 90 to 99 per cent (ELSD).

On average, up to 20 per cent of all fractions from plant extracts are 90 to 99 per cent pure (ELSD), and from marine organisms, up to 30 per cent are 90 to 99 per cent pure (ELSD).

As well as these highly purified compounds, the user will usually find a large number of fractions with compounds whose purity levels are between 50 and 90 per cent in ELSD detection. Results vary depending on the extract and the examined organism. (The purity levels quoted here were calculated using the 100 per cent method with ELSD detection, as UV detection does not provide reliable purity levels due to different adsorption coefficients.)

SEPMATIX



INTRODUCTION TO SEPMATIX SYSTEMS

Shortcomings of HPLC ...

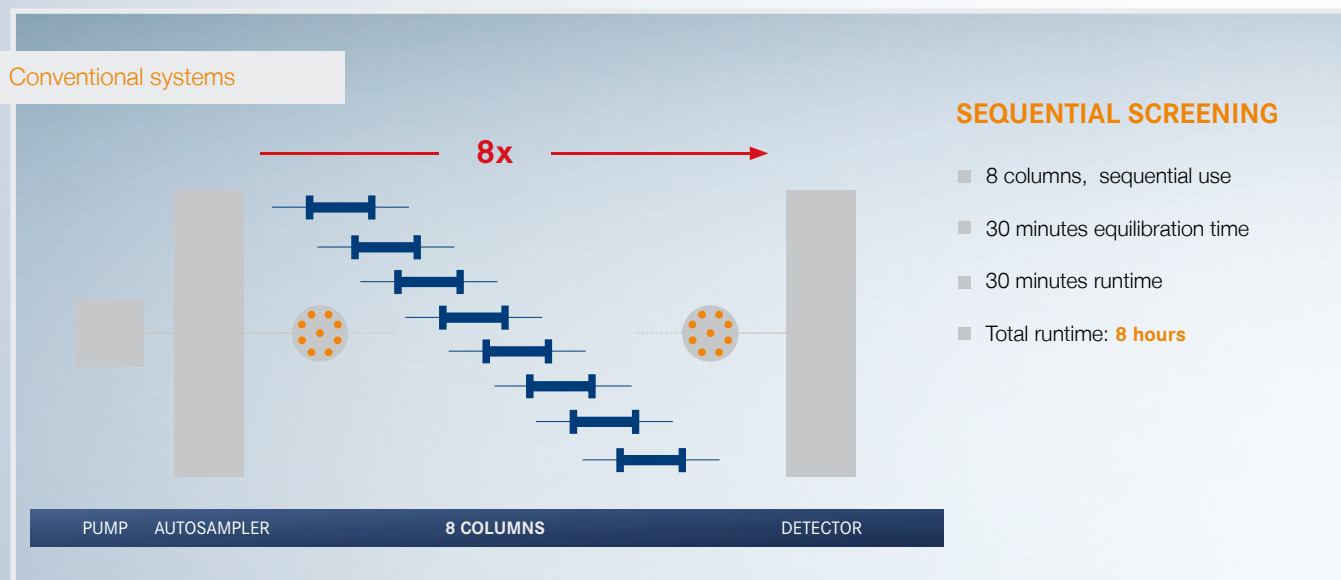
Even though HPLC technology is well established and widely used today in many fields of pharmaceutical and biotechnology research, there are physical limitations which affect the level of throughput.

Using large numbers of automated HPLC systems in parallel is not an effective solution, because they are so costly, take up so much space and require so much time and effort to operate. They also require considerable maintenance. For example, if eight columns

are used to separate the samples, then maintenance will not only be required for these columns, but it will also be required for a series of HPLC pumps, autosamplers and detectors.

HPLC systems that use higher pressure (over 400 bar) to deliver quicker results have their own limitations. This is because they need very pressure-resistant column materials in order to provide good separation results – but many of the materials used for HPLC technology are not yet available in a pressure-resistant form, or are simply not suitable. As a result, many of these high-pressure HPLC systems are used like conventional HPLC systems and therefore do not contribute to increasing throughput.

Conventional systems



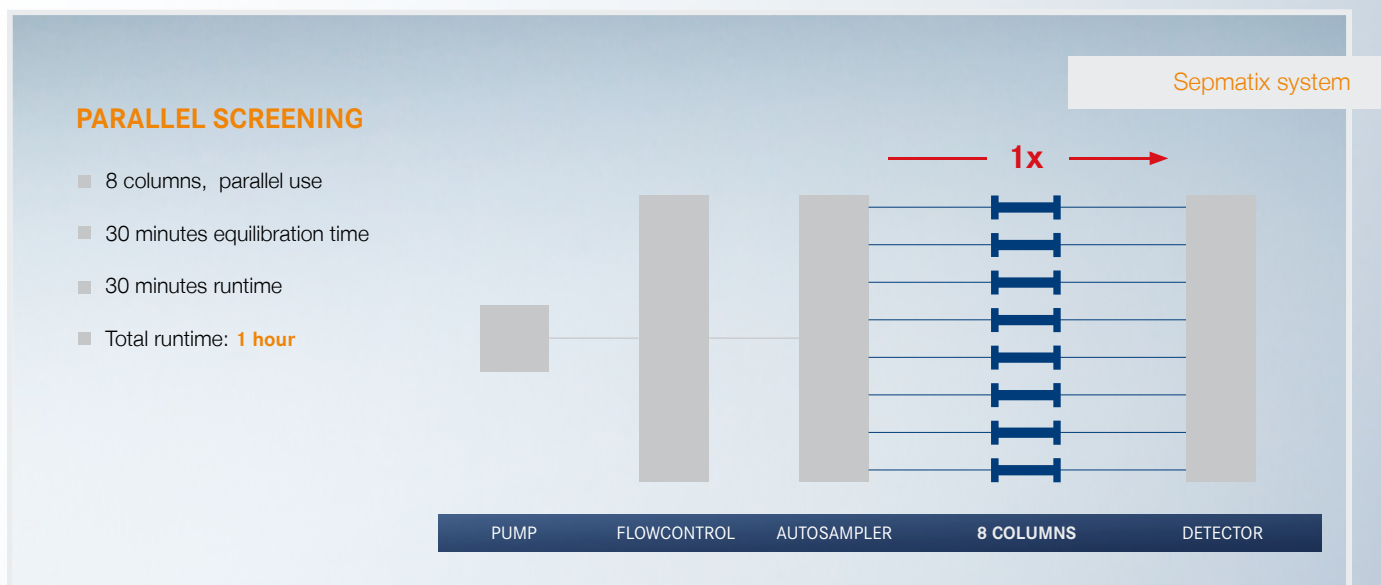
... can be solved by parallel technology

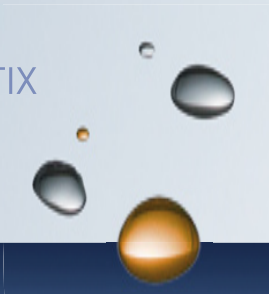
The **8x parallel Sepmatix HPLC system** from Sepiatec only uses one external HPLC pump. The flow is separated by the patented Sepmatix FlowControl into eight channels, and the flow in each channel is precisely measured and regulated throughout the entire run. Together with an autosampler and an 8x parallel working detector, the result is an unbelievably compact HPLC system, which will instantly enhance the throughput of every research and development laboratory eight times over.

It is not necessary to spend time adapting methods to the new system or to purchase any new costly HPLC columns.

Different designs of the Sepmatix 8x parallel HPLC system are available for applications such as chiral column screening, protein screening, method development, or with an 8x FractionCollector for preparative work.

The user can continue to use all the methods and separation materials that they were using with their conventional HPLC systems.





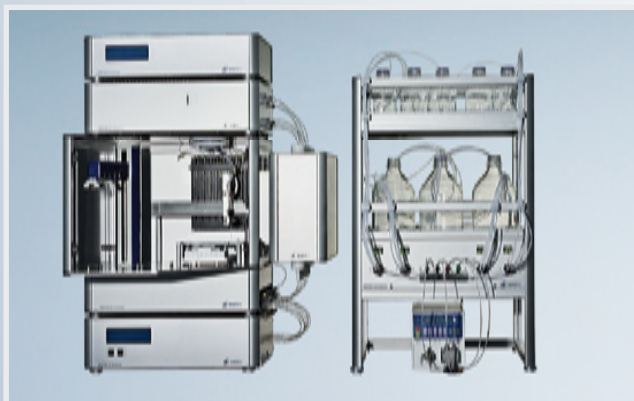
CHIRAL COLUMN SCREENING

In chiral column screening, it is essential that the conditions for separating chiral substances are found quickly and effectively. As a result, many large pharmaceutical companies have recently decided to equip their chiral column screening departments with an 8x Sepmatix system.

The **8x Sepmatix system for chiral column screening** can separate a substance on eight different chiral separation columns simultaneously. This significantly increases sample throughput.

The system consists of three modules: an 8x FlowControl low-viscosity version with flow rates of between 0.25 to 1.50 ml/min; an autosampler with syringe pump which injects samples from standard microtiter plates or deep-well microtiter plates onto eight columns (also suitable for vial racks); and an 8x Diode Array Detector with eight analytical flow cells applicable for the spectral range of 200 to 600 nanometres.

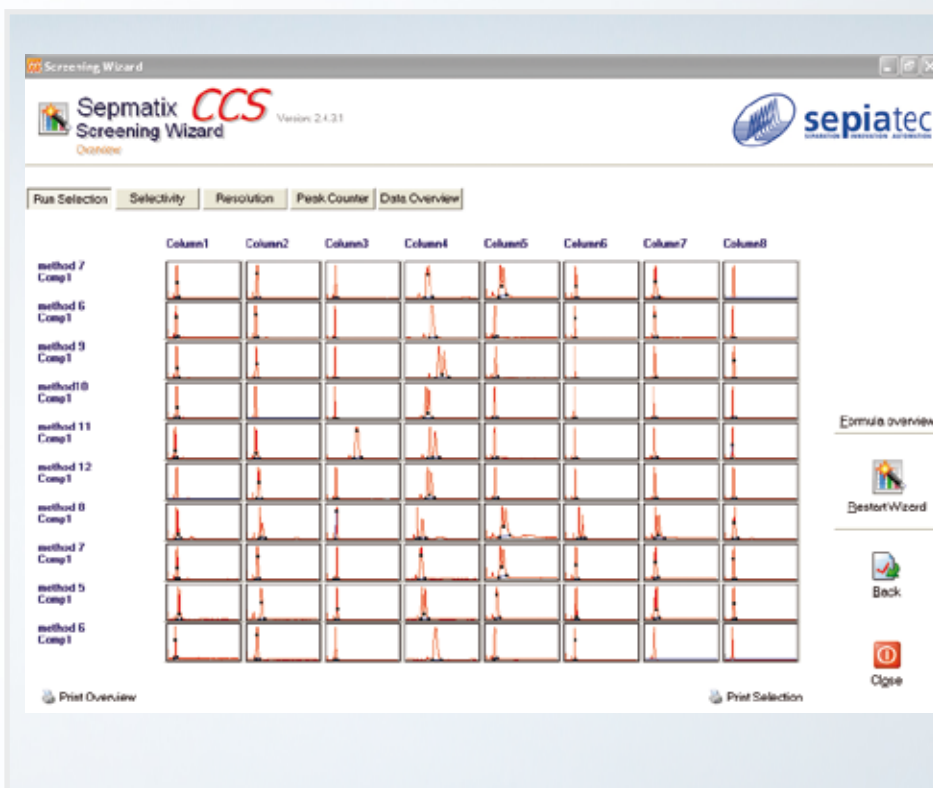
The required space for the 8x Sepmatix system for chiral column screening is only 55 x 55 x 90 centimetres (W x D x H).



The 8x Sepmatix system for chiral column screening can be fitted with the Sepmatix EluentRack, which is designed for a maximum of four Solvent SelectionValves (each with six positions) and up to 24 solvent bottles (1 litre) or 18 flasks (2.5 litres). The required space for the Sepmatix EluentRack is 55 x 55 x 90 centimetres (W x D x H).

CHIRAL COLUMN SCREENING SOFTWARE

The **Chiral Column Screening Wizard Software** developed by Sepiatec offers many different options and parameters, such as selectivity, capacity, resolution, and data overview for the analysis of chromatograms.



The software can display up to 80 chromatograms at once, together with the associated columns and method terms. This very useful function provides the user with an excellent overview, so that they can quickly make a decision as to which columns and run conditions are showing the best results.



PROTEIN SCREENING

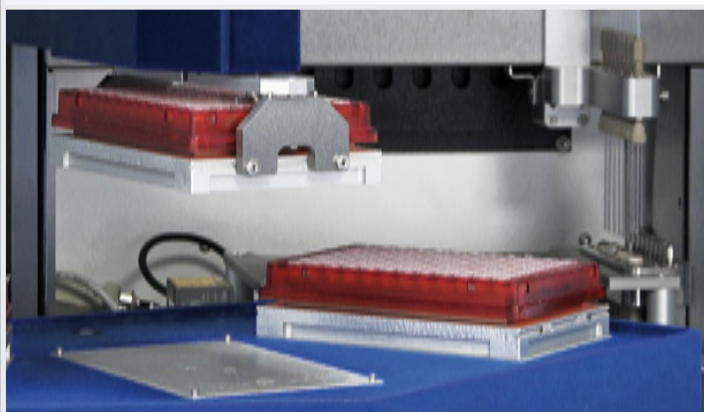
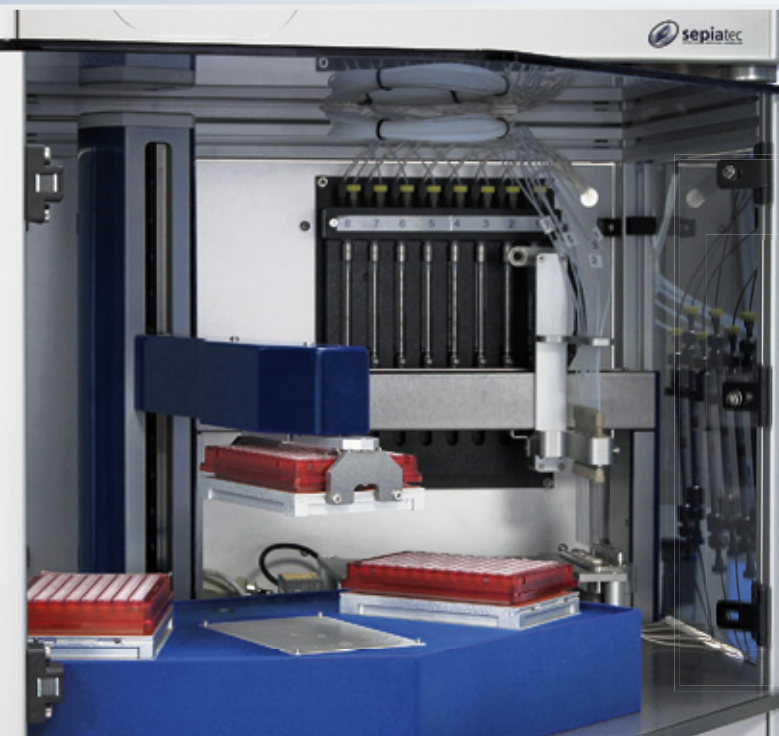
The **8x Sepmatix system for protein screening** is designed to preserve the biologically active structure of peptides and proteins during the separation process.

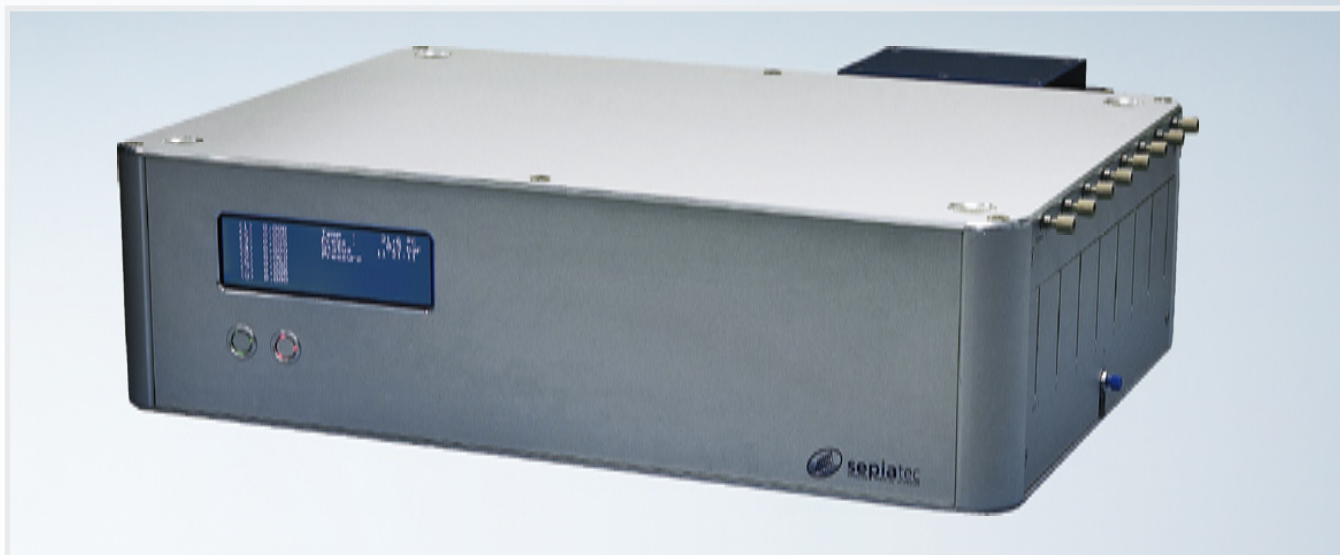
The system consists of three modules: an 8x FlowControl, an 8x Autosampler and an 8x Diode Array Detector. The system's autosampler has three positions for 96 shallow well microtiter plates, which can be cooled to as low as 4 to 8 degrees Celsius. The sample is injected simultaneously into the eight separation columns.

If required, the 8x Sepmatix system can be fitted with a Column-Oven designed to cool down or heat up eight columns independently from each other within a range of between 5 and 70 degrees Celsius.

Internal or external barcode readers are available for recording microtiter plates with barcode labels.

For preparative applications, Sepiatec offers an 8x FractionCollector. This compact system combines eight independent FractionCollectors in one. For each of the eight channels in the 8x Sepmatix system, there is one FractionCollector available. This can be loaded with up to 12 standard or deep-well microtiter plates. The 8x FractionCollector can therefore be loaded with up to 96 microtiter plates.

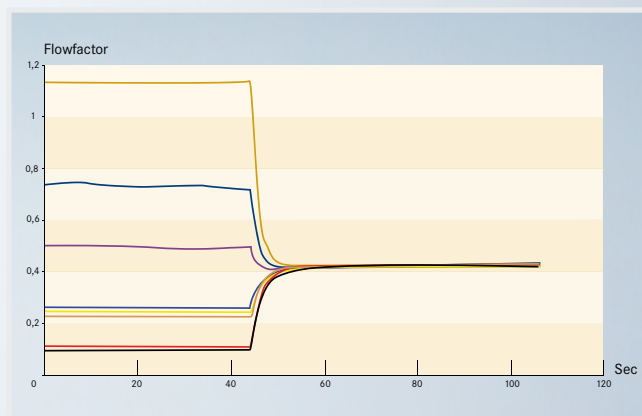




FLOWCONTROL

The **Sepmatec 8x FlowControl module** guarantees constant flow rates in up to eight channels, while using just one HPLC pump (diagram). The FlowControl is a key part of the Sepmatec system, but can be used as a stand-alone unit to adjust the flow of existing HPLC or LC-MS systems if required.

Sepiatec also offers a 4x FlowControl four channel unit. Both the 8x and the 4x FlowControl systems are available as an **analytical version** (with flow rates from 0.25 to 1.5 ml/min per channel), a **semiprep version** (1.5 to 6.0 ml/min per channel) and a **prep version** (6.0 to 20.0 ml/min per channel).



ORDER INFORMATION

Sepmatix Systems

Art. No.	Device
200-01	8x Sepmatix System Analytical Flow rates 0.25-1.50 ml/min, parallel injection
200-05	8x Sepmatix System Chiral Column Screening Flow rates 0.25-1.50 ml/min, parallel injection
200-07	8x Sepmatix System Protein Screening Flow rates 0.25-1.50 ml/min, parallel injection

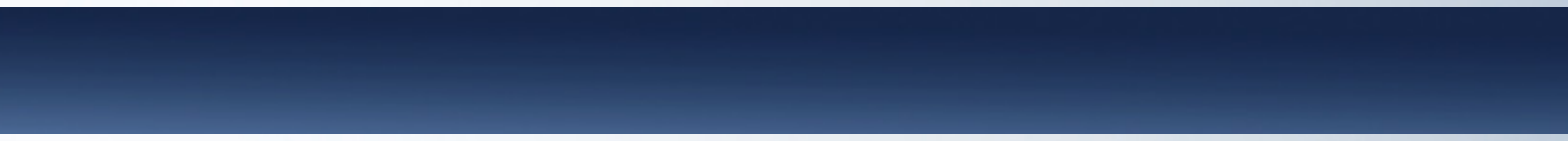
FlowControl Modules

220-01	Sepmatix 8x FlowControl Analytical
220-02	Sepmatix 8x FlowControl Semiprep
220-03	Sepmatix 8x FlowControl Prep


Sepmatix Systems Accessories

230-01	Sepmatix 8x FractionCollector, big Up to 8 x 12 microtiter plates
250-01	Sepmatix 8x ColumnOven
250-08	Sepmatix Solvent SelectionValve 6 inlet positions
250-20	Sepmatix EluentRack Capacity for 24 x 1l bottles or 18 x 2.5l flasks
250-40	Sepmatix ColumnSelector Up to 40 columns can be used with the Sepmatix System
260-01	Analogue output card The connection to other chromatography data handling systems
270-01	Barcode scanner internal device For microtiter plates
400-06	Chiral Column Screening Software

Details of other systems, configurations and accessories available on request



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