

Preparative Chromatography

Overview

Liquid chromatography has long become established as the method of choice for the separation and analysis of all kinds of mixtures which arise naturally, either due to complex environmental conditions or as a result of a chemical manufacturing process. KNAUER offers modular HPLC systems for analytical as well as preparative and continuous chromatography.

For satisfactory results in analytical chromatography it is generally necessary to operate with smaller bore columns, moderately low flowrates and low injection quantities.

Preparative chromatography scales up this analytical process to allow the isolation of a maximum amount of a required product at a defined purity level in the minimum of time.

Scale-up

The scale-up process generally occurs in two separate steps. Step 1 is to increase column dimensions and flowrate while trying to maintain the linear flow conditions from the analytical application. Table 1 below shows the impact of column size on volumetric flowrate:

Column (mm)	Flow rate (ml/min)	Cross section (cm ²)	Linear velocity (m/min)
250 x 4	2	0.1257	16
250 x 8	8	0.5027	16
250 x 16	32	2.0109	16
250 x 32	128	8.0435	16
250 x 40	200	12.568	16
250 x 62	480	30.195	16

Step 2 in the scale-up process is often to increase the amount of sample injected in order to allow operation of the system under column overload conditions thus obtaining benefits in terms of system productivity.

Preparative or Semi-preparative Systems

The table below lists the main system parameters for definition of a system whereby the border between semi-preparative and preparative systems is generally not clearly defined.

	Analytical	Semi-preparative	Preparative
Column Length (mm)	120 - 250	120 - 250	120 - 250
Column Diameter (mm)	2 - 4.6	8 - 16	20 - 62
Flow Rates (ml/min)	0.1 - 2	5 - 50	100 - 1000
Cell path length (mm)	10	3	0.5 - 2
Tubing	1/16"	1/16"	1/8"

System and Application Design

Analytical and preparative HPLC systems possess in principle a similar design but have completely different system requirements, particularly with regard to the pumping systems. The Knauer Smartline 1800 Pump offers flowrates up to 1000 ml per minute with 4 different pump heads for optimum combination of flow and pressure capability.

As the process scale increases, the throughput will also increase and the eluent consumption will become a significant economic factor. For this reason an application for preparative chromatography should always be isocratic if at all possible. This permits the use of solvent recycling mechanisms which are not practically possible with gradient methods. Knauer offers valves for fraction collection and recycling applications as well as gradient options for very critical applications.