

Reagents for Pharma Industry

Chapter 4



PanReac 
AppliChem
ITW Reagents



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About Us

The Origin

ITW Illinois Tool Works Inc. (NYSE: ITW) is a global industry company that delivers specialized expertise, innovative thinking and value-added products to meet critical customer needs in a variety of industries.

ITW, with approximately 14 billion dollars in global revenues, operates 7 major segments with businesses in 58 countries that employ approximately 50,000 employees. The company has a broad portfolio of more than 17,000 global patents and patent applications.

The ITW Reagents Division

In 2010, the ITW Reagents division was born integrated by the companies Panreac Química SLU (Spain) and Nova Chimica Srl (Italy), and later on by AppliChem GmbH (Germany). The division offers the highest quality and innovative products for analysis, research and production applications.

ITW Reagents markets its products worldwide through an extensive distribution network to more than 80 countries under the PanReac AppliChem brand. It has two production plants in Darmstadt (Germany) and Barcelona (Spain).



We are Everywhere

We can say that almost all products subject to human manipulation have undergone chemical analysis that guarantees their physical and chemical properties. Food, agrifood, medicines, cosmetics... and so many other products are subjected to chemical analysis. Our reagents can be found in any quality control and research laboratory.



Our range of Laboratory Chemicals include:

Analytical reagents
Reagents for volumetric analysis
Reagents and solvents for general applications
Reagents and solvents for HPLC
Reagents and solvents for GC
Reagents for metallic traces analysis
Analytical standards
Reagents and solvents for specific applications
Products for clinical diagnosis
Products for microbiology

Our range of Laboratory Biochemicals cover:

Cell Biology / Cell Culture
Protein Biochemistry and Electrophoresis
Nucleic Acid Biochemistry
General Biochemicals and Biological Buffers
Special Biochemicals

Service & Benefits

Exceptional know-how and a wide range of chemicals and biochemicals for a great diversity of applications.

European production committed to corporate social responsibility (CSR).

Efficient global distribution network to export our products worldwide to more than 80 countries.

Qualified management team fully committed to our business project.

Excellence

Our products are strictly controlled in our laboratories and meet the highest quality requirements. A multi-site Integrated Management System for Quality, Environment and Safety is implemented in all activities and processes.

ISO 9001:2015

ISO 14001:2015

OHSAS 18001:2007



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Introduction

The **Pharmaceutical Industry** discovers, develops, produces, and markets drugs or **pharmaceutical drugs** for use as medications.

Pharmaceutical companies may deal in **generic** or **brand medications** and medical devices.

They are subject to a variety of **laws** and **regulations** that govern the patenting, testing, safety, efficacy and marketing of drugs.

The pharmaceutical industry is largely driven by **scientific discovery** and **development**, in conjunction with **toxicological** and **clinical experience**.



Major differences exist between **large organizations** which engage in a broad range of drug discovery and development, manufacturing and quality control, marketing and sales and **smaller organizations** which focus on a specific aspect.



Most multinational pharmaceutical companies are involved in all these activities; however, they may specialize in one aspect based upon local market factors. Academic, public and private organizations perform scientific **research to discover and develop new drugs**. The biotechnology industry is becoming a major contributor to innovative pharmaceutical research. Often, collaborative agreements between research organizations and large pharmaceutical companies are formed to explore the potential of new drug substances.

Active drug substances (APIs, Active Principle Ingredient) and **inert materials** (Excipients) are combined **during pharmaceutical manufacturing** to produce dosage forms of medicinal products (e.g. tablets, capsules, liquids, powders, creams and ointments). Drugs may be categorized by their manufacturing process and therapeutic benefits.



The different pharmaceutical manufacturing processes each have their own **environmental issues** and the wastes must be treated and controlled. **For example:**

- During **fermentation process**, the spent fermentation broth contains sugars, starches, proteins, nitrogen, phosphates and other nutrients with high biochemical oxygen demand (BOD), chemical oxygen demand (COD) and total suspended solids (TSS) with pH values ranging from 4 to 8.
- Also, wastes from **chemical synthesis** are complex due to the variety of hazardous materials, reactions and unit operations. These waste waters are high in BOD, COD and TSS, with varying acidity or alkalinity and pH values ranging from 1 to 11.



The **analysis laboratories** play a fundamental role in the pharmaceutical industries. **They are key pieces in:**



- Discovery and improvement of a **drug**.
- Development and optimization of **manufacturing processes**.
- **Quality control** of raw materials, intermediates and finished products.
- Quality control of **wastes**.

!

Depending on the type of analysis in which they are involved, **different types of laboratories** can be distinguished within the same pharmaceutical company. Besides, the **type of analysis** and the techniques used may be different (as shown on the next page).

In any case, the methods of analysis must be strictly validated and follow the requirements set by the **Pharmacopoeias** (Ph. Eur., USP, etc.) both in the analysis protocols and in the quality of the reagents to be used.

Our **portfolio** includes a wide range of products such as solvents, acids, bases and salts indicated for general analytical applications that **fulfil the requirements indicated in the Pharmacopoeias** (Ph. Eur. or USP) for the reagents to be used for analytical purposes.



Types of Laboratories versus Methods of Analysis

Facility		R&D Centre		Manufacturing Plant Quality Control			Wastewater Plant
Laboratory		New molecules / Improvements of existing products	Analytical development	Raw Material (excipients & APIs)	In-process (intermediate product)	Final product	Water quality control
Methods of analysis	Chapter						
Amino acid analysis	5			●	●	●	
Ammonium	6/7						●
Approximate pH of solutions	1		●	●	●	●	●
Assay: Protein (Kjeldahl)	6		●	●			
Assay: Titration	6		●	●			
Assay: Water (KF)	6		●	●	●	●	
Atomic Absorption spectroscopy	2		●	●			
Biological assays	3		●	●			
Biological tests	3			●		●	
Clarity and opalescence of liquids	1		●	●		●	
Chlorinated compounds	7						●
Conductivity	1		●	●			
Degree of Coloration of Liquids	1		●	●			
Detergents (Surfactants)	7						●
Dissolution Test	1					●	
Electrophoresis	5	●	●	●	●	●	
Gas Chromatography	4	●	●	●		●	
ICP	2		●	●			
Identification	6		●	●		●	
IR	2	●	●	●		●	
Limit tests	6		●	●			
Liquid Chromatography	4	●	●	●		●	
Molecular mass distribution in dextrans	5			●	●		
Organic compounds (COD, DBO5, TOC)	7						●
Peptide identification by NMR spectrometry	5	●	●	●	●	●	
Peptide mapping	5	●		●	●	●	
Phosphates	6/7						●
Potentiometric determination of pH	1		●	●	●	●	●
Residual catalyzers (Metals, Cyanides)	7						●
Suspended matter	7						●
Thin Layer Chromatography	4	●	●	●			
UV	2	●	●	●			
Synthesis*	8	●					

*not a method of analysis but reagents and solvents involved in synthesis procedures.

In the following sections we will describe the most common methods of analysis indicated in the pharmacopoeias and offer the most appropriate reagents for each method.



Chromatography

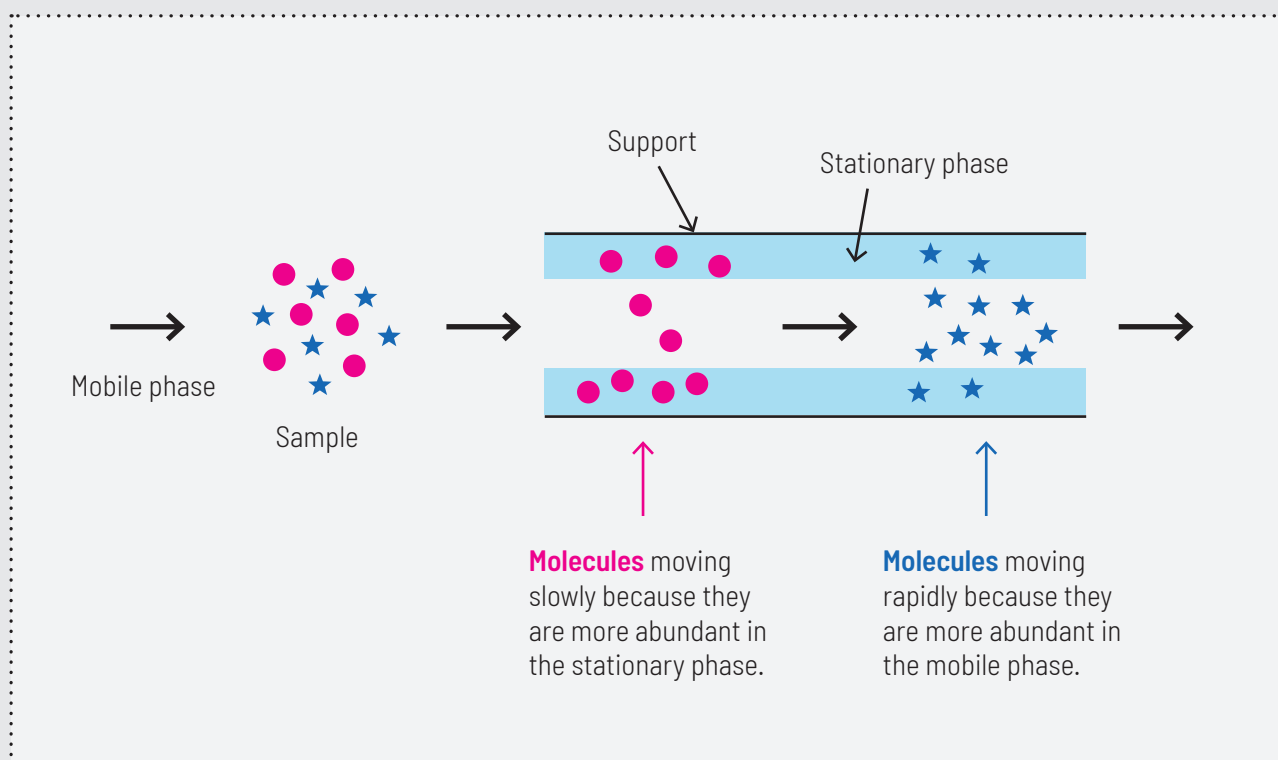
Technique and Parameters

Chromatography is a technique in analytical chemistry used to separate, identify, and quantify each component in a mixture.

It is a physical method of separation, in which the components to be separated are distributed between two phases, one of which is stationary while the other moves in a definite direction.

The **stationary phase** may be a solid or a liquid supported on a solid or a gel. The stationary phase may be packed in a column, spread as a layer, or distributed as a film, etc.

The **mobile phase** may be gaseous or liquid or supercritical fluid.



The separation may be based on adsorption, mass distribution (partition), ion-exchange, etc. or may be based on differences in the physico-chemical properties of the molecules such as size, mass, volume, etc.

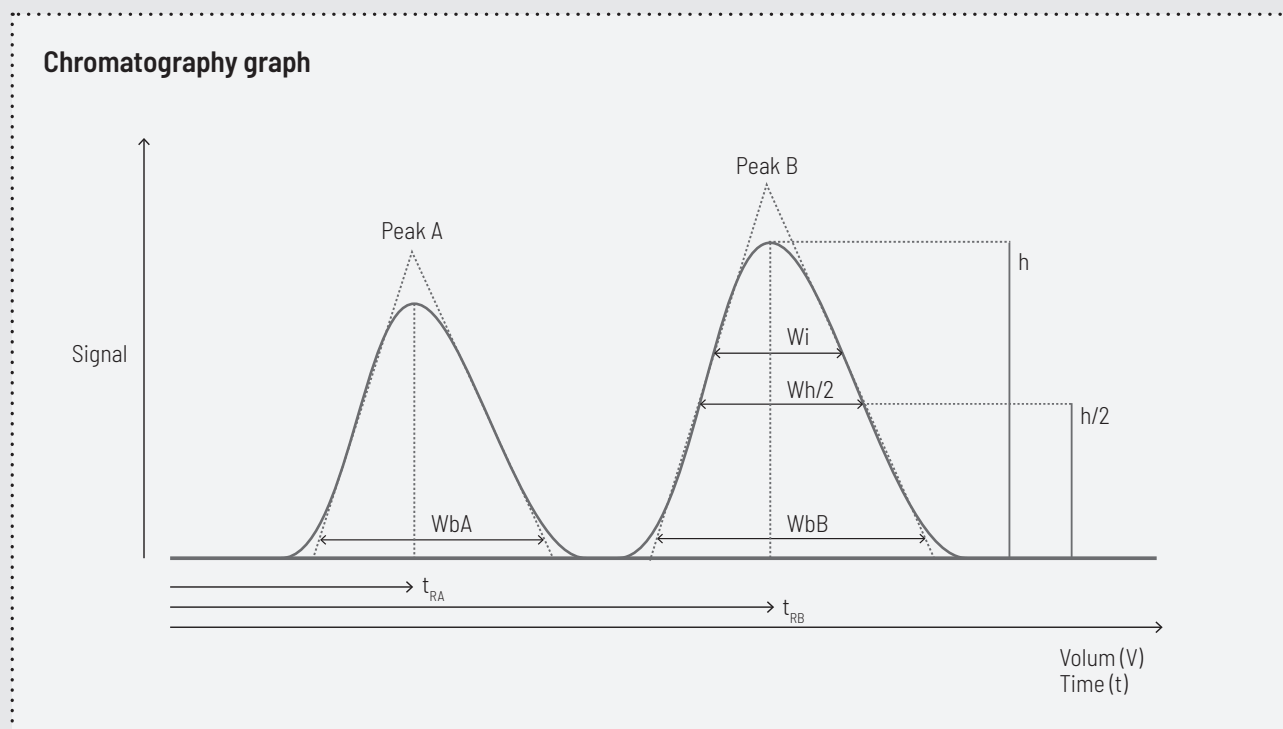
Chromatography may be either preparative or analytical. The purpose of preparative chromatography is to separate the components of a mixture for later use, and is thus a form of purification. Analytical chromatography is usually performed with smaller amounts of material and is used to establish the presence or measure the relative proportions of analytes in a mixture. The two are not mutually exclusive.

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The analytes, once separated can be identified in a detector which response is represented in a graphical, called **Chromatogram**. Idealized chromatograms are represented as a sequence of Gaussian peaks on a baseline.



Some of the **parameters** evaluated in Chromatography:

Peak

The portion of a chromatogram recording the detector response when a single component (or two or more unresolved components) is eluted from the column.

The peak may be defined by the peak area, or the peak height (h) and the peak width at half-height ($W_{h/2}$) or the peak height (h) and the peak width between the points of inflection (W_i).

Retention time (t_R)

Time required for elution of a component.

Retention volume (V_R)

Volume of the mobile phase required for elution of a component. It may be calculated from the retention time and the flow rate (F) in milliliters per minute using the following equation:

$$V_R = t_R \times F$$

Resolution (R_s)

In general, resolution is the ability to separate two signals. In terms of chromatography, this is the ability to separate two peaks.

Resolution is calculated using the separation of two peaks in terms of their average peak width at the base ($t_{RA} < t_{RB}$). It may be calculated using the following equation:

$$R_s = 1.18 (t_{RB} - t_{RA}) / (W_{A,h/2} + W_{B,h/2})$$

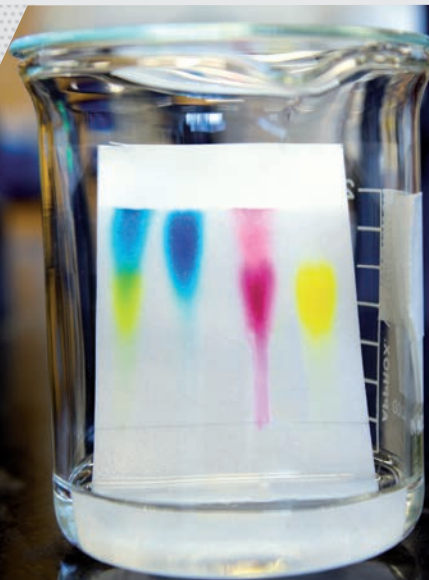
The most important thing in Chromatography is to obtain the **optimum resolution** in the shortest possible time.

In this chapter we will talk about three types of separation techniques: TLC, HPLC and GC and the recommended reagents and qualities that PanReac AppliChem can offer for each type of technique.

Thin-Layer Chromatography

Thin-Layer Chromatography (TLC) is a separation technique in which a stationary phase consisting of a suitable material is spread in a thin, uniform layer on a support (**plate**) of glass, metal or plastic.

It is applicable to substances or their derivatives which are non volatiles at room temperature.



The separation is based on adsorption, partition, ion-exchange or on a combination of these mechanisms and is carried out by migration of solutes (**solutions of analytes**) in a solvent or a suitable mixture of solvents (**mobile phase or eluent**) through the thin-layer (**stationary phase**).

Apparatus

The **apparatus** consists of:

- A **plate**
- A chromatographic **tank**
- A fluorescence **detector** device
- **Visualization** device and reagents

Plate

TLC plates are prepared by mixing the adsorbent, such as silica gel, with a small amount of inert binder such as calcium sulfate (gypsum) and water. This mixture is spread as a thick slurry over a non-reactive carrier sheet, usually glass, thick aluminium foil, or plastic. The resultant plate is dried and activated by heating in an oven for 20 minutes at 120 °C. The thickness of the adsorbent layer is typically around 0.1 – 0.25 mm for analytical purposes and around 0.5 – 2.0 mm for preparative TLC.

Chromatographic tank

It is a vessel with a flat bottom or a twin trough chamber, of inert, transparent material, of a size suitable for the plates used and provided with a tightly fitting lid. For horizontal development the tank is provided with a trough for the mobile phase and it additionally contains a device for directing the mobile phase to the stationary phase.

Fluorescence detector device is one of the visual detection of the results, can measure direct fluorescence or inhibition of fluorescence.

Visualization device and reagents

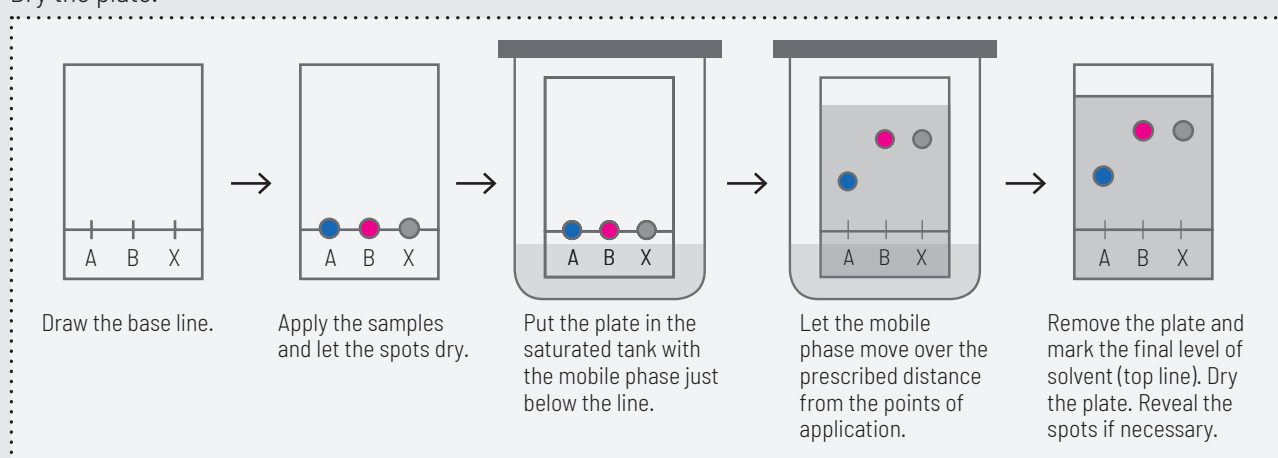
Suitable devices are used for derivatization to transfer to the plate reagents by spraying, immersion or exposure to vapor and, where applicable, to facilitate heating for visualization of separated components.



Method

It is necessary to apply the samples (in spots with a maximum diameter of 5 mm) with at least 10 mm between each sample on a parallel line to the lower edge of the plate.

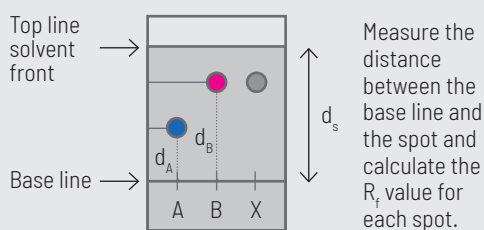
Once the sample has been applied to the plate and the solvent from the samples has evaporated, it is introduced into the tank saturated with the solvent or solvent mixture (known as the mobile phase). Because there are different analytes on the TLC plate, the analytes ascend at different rates, thus achieving separation. The mobile phase has different properties from the stationary phase, normally the difference is the polarity. The mobile phase may be a mixture, allowing chemists to fine-tune the bulk properties of the mobile phase. Remove the plate when the mobile phase has moved over the prescribed distance, measured between the points of application and the solvent front. Dry the plate.



After the experiment, the spots are visualized. Often this can be done by simply projecting ultraviolet light onto the sheet; the sheets are treated with a phosphor, and dark spots appear on the sheet where compounds absorb the light that strikes a certain area. Specific reagents can also be used to visualize spots.

Calculating the R_f value

To quantify the results, the distance travelled by the substance is divided by the distance traveled by the solvent from the point of application. (The mobile phase must not be allowed to reach the end of the stationary phase). This ratio is called the **retardation factor (R_f)**. In general, a substance whose structure resembles the stationary phase will have low R_f , while one that has a structure similar to the mobile phase will have high retardation factor. Retardation factors are characteristic, but will change depending on the exact condition of the mobile and stationary phase. For this reason, a sample of a known compound is usually applied to the sheet before running the experiment.



The retardation factor (R_f) can be used to identify the components of a mixture (solutes).

$$R_f = \frac{\text{distance travelled by solute}}{\text{distance travelled by solvent front}}$$

$$R_f = \frac{d_x}{d_s}$$

$$R_f(A) = \frac{d_A}{d_s}$$

$$R_f(B) = \frac{d_B}{d_s}$$

The highest R_f value is the substance with the least interaction with plate.

Thin-layer chromatography can be used to monitor the progress of a reaction, identify compounds present in a given mixture, and determine the purity of a substance. Specific examples of these applications include: analysis of ceramides and fatty acids, detection of pesticides or insecticides in food and water, analysis of the dye composition of fibers in forensics, assaying the radiochemical purity of radiopharmaceuticals, or identification of medicinal plants and their components.

Solvents for mobile phase in TLC

Product name	Code	Package
Acetic Acid 96% for analysis	122703.1611	1000 ml
	122703.1612	2.5 L
Acetone (Reag. Ph. Eur.) for analysis, ACS, ISO	131007.1611	1000 ml
	131007.1211	1000 ml
	131007.1612	2.5 L
	131007.1212	2.5 L
	131007.1214	5 L
	131007.0515	10 L
	131007.0716	25 L
	131007.0516	25 L
	131007.0537	30 L
Acetonitrile (Reag. Ph. Eur.) for analysis, ACS	131881.1611	1000 ml
	131881.1612	2.5 L
Benzene (Reag. Ph. Eur.) for analysis, ACS, ISO	131192.1611	1000 ml
	131192.1612	2.5 L
	131192.0616	25 L
1-Butanol (Reag. Ph. Eur.) for analysis, ACS, ISO	131082.1611	1000 ml
	131082.1612	2.5 L
	131082.1214	5 L
n-Butyl Acetate (Reag. USP, Ph. Eur.) for analysis, ACS	131202.1611	1000 ml
	131202.0619	200 L
Chloroform stabilized with ethanol (Reag. Ph. Eur.) for analysis, ACS, ISO	131252.1611	1000 ml
	131252.1612	2.5 L
Cyclohexane (Reag. Ph. Eur.) for analysis, ACS, ISO	131250.1611	1000 ml
	131250.1612	2.5 L
	131250.0314	5 L
	131250.0316	25 L
Dichloromethane stabilized with ~ 20 ppm for amylene for analysis, ACS, ISO	131254.1611	1000 ml
	131254.1612	2.5 L
	131254.1714	5 L
	131254.0515	10 L
	131254.0537	30 L
	131254.0619	200 L
N,N-Dimethylformamide (Reag. Ph. Eur.) for analysis, ACS, ISO	131785.1611	1000 ml
	131785.1612	2.5 L
	131785.1214	5 L
	131785.0716	25 L
Dimethyl Sulfoxide (Reag. Ph. Eur.) for analysis, ACS	131954.1611	1000 ml
	131954.1612	2.5 L
	131954.1214	5 L
	131954.0715	10 L

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Product name	Code	Package
1,4-Dioxan stabilized with ~ 25 ppm of BHT (Reag. Ph. Eur.) for analysis, ACS, ISO	131296.1611	1000 ml
	131296.0616	25 L
Ethanol absolute for analysis, ACS, ISO	131086.1611	1000 ml
	131086.1211	1000 ml
	131086.1612	2.5 L
	131086.1212	2.5 L
	131086.1214	5 L
	131086.1315	10 L
	131086.0716	25 L
	131086.0516	25 L
Ethyl Acetate (Reag. Ph. Eur.) for analysis, ACS, ISO	131318.1611	1000 ml
	131318.1211	1000 ml
	131318.1612	2.5 L
	131318.1212	2.5 L
	131318.1214	5 L
	131318.0515	10 L
	131318.0537	30 L
Ethylene Glycol mono-Methyl Ether for analysis, ACS	131897.1611	1000 ml
n-Heptane for analysis	122062.1611	1000 ml
	122062.1612	2.5 L
	122062.0314	5 L
	122062.0619	200 L
n-Hexane (Reag. USP, Ph. Eur.) for analysis, ACS	132063.1611	1000 ml
	132063.1612	2.5 L
Isobutanol (Reag. Ph. Eur.) for analysis, ACS	131089.1611	1000 ml
	131089.0716	25 L
Isooctane (Reag. Ph. Eur.) for analysis, ACS	132064.1611	1000 ml
	132064.1612	2.5 L
	132064.0314	5 L
Methanol (Reag. Ph. Eur.) for analysis, ACS, ISO	131091.1611	1000 ml
	131091.1211	1000 ml
	131091.1612	2.5 L
	131091.1212	2.5 L
	131091.1214	5 L
	131091.0716	25 L
	131091.0537	30 L
4-Methyl-2-Pentanone (Reag. Ph. Eur.) for analysis, ACS	131430.1611	1000 ml
	131430.0716	25 L
1-Propanol (Reag. USP, Ph. Eur.) for analysis, ACS	131885.1611	1000 ml
	131885.1211	1000 ml
	131885.1612	2.5 L
	131885.0716	25 L

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Product name	Code	Package
2-Propanol (Reag. Ph. Eur.) for analysis, ACS, ISO	131090.1611	1000 ml
	131090.1211	1000 ml
	131090.1612	2.5 L
	131090.1212	2.5 L
	131090.1214	5 L
	131090.0515	10 L
	131090.0716	25 L
Pyridine (Reag. Ph. Eur.) for analysis, ACS	131457.1611	1000 ml
	131457.1612	2.5 L
	131457.0716	25 L
Tetrahydrofuran stabilized with ~ 300 ppm of BHT for analysis, ACS	133537.1611	1000 ml
	133537.1612	2.5 L
	133537.0314	5 L
	133537.0537	30 L
Toluene (Reag. Ph. Eur.) for analysis, ACS, ISO	131745.1611	1000 ml
	131745.1612	2.5 L
	131745.0314	5 L
	131745.0616	25 L
Water for analysis, ACS	131074.1211	1000 ml
	131074.1212	2.5 L
	131074.1214	5 L
	131074.1315	10 L
	131074.0716	25 L
	131074.0718	60 L
	131074.0719	200 L
Xylene, mixture of isomers (Reag. Ph. Eur.) for analysis, ACS, ISO	131769.1611	1000 ml
	131769.2711	1000 ml
	131769.1612	2.5 L
	131769.0314	5 L
	131769.0616	25 L
	131769.0619	200 L

HPLC and Spectroscopy grade solvents (product codes beginning with 36) are recommended if column adsorption after TLC is necessary.



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Visualization reagents

Product name	Code	Package
Bromocresol Green for analysis, ACS	131759.1604	5 g
	131759.1606	25 g
2',7'-Dichlorofluorescein (Reag. Ph. Eur.) for analysis, ACS	133606.1604	5 g
Ninhydrin for analysis, ACS	132362.1605	10 g
	132362.1608	100 g
	132362.1611	1000 g
Phosphomolybdic Acid x-hydrate for analysis, ACS	131031.1606	25 g
	131031.1608	100 g



Liquid Chromatography

In **Liquid Chromatography (LC)** the mobile phase is a liquid which percolates through a stationary phase contained in a column. The stationary phase is either a solid, porous, surface-active material in small-particle form, or a liquid which is coated onto micro-particulate beads of an inert solid support (usually silica).



In **HPLC** (High Performance Liquid Chromatography; formerly called High-Pressure Liquid Chromatography) the mobile phase containing the sample is pressurized through the column.

UHPLC (Ultra High Performance Liquid Chromatography) is a special version of HPLC that allows a very fast analysis and a better separation than in HPLC. Column particle sizes are less than 2 μm (in HPLC the particle sizes are generally 5 μm) and needs higher pump pressures, up to 100 MPa, compared with 40 MPa (400 atm) in HPLC.

There are many **stationary phases** used in LC that involve different **mobile phases** and also different **mechanisms of separation** that lead to classifying the LC in different types, the most common being:

- **Normal Phase Chromatography (NP):** this method separates analytes based on their affinity for a polar stationary surface such as silica or alumina, hence it is based on analyte ability to engage in polar interactions (such as hydrogen-bonding or dipole-dipole type of interactions) with the sorbent surface. It uses a non-polar, non-aqueous mobile phase (e.g. chloroform), and works effectively for separating analytes readily soluble in non-polar solvents.
- **Reversed Phase Chromatography (RP):** this method has a non-polar stationary phase and an aqueous, moderately polar mobile phase (common mobile phases include any miscible combination of water with various organic solvents, the most commonly used being acetonitrile and methanol). One common stationary phase is a silica which has been surface-modified with RMe_2SiCl , where R is a straight chain alkyl group such as $\text{C}_{18}\text{H}_{37}$ or C_8H_{17} . It operates on the principle of hydrophobic interactions.
- **Size Exclusion Chromatography (SEC):** also known as gel permeation chromatography or gel filtration chromatography, it separates particles on the basis of molecular size. SEC is used primarily for the analysis of large molecules such as proteins or polymers. SEC works by trapping these smaller molecules in the pores of a particle.
- **Ion Exchange Chromatography (IEC, IC, IEX):** retention is based on the attraction between solute ions and charged sites bound to the stationary phase. Solute ions of the same charge as the charged sites on the column are excluded from binding, while solute ions of the opposite charge of the charged sites of the column are retained on the column.

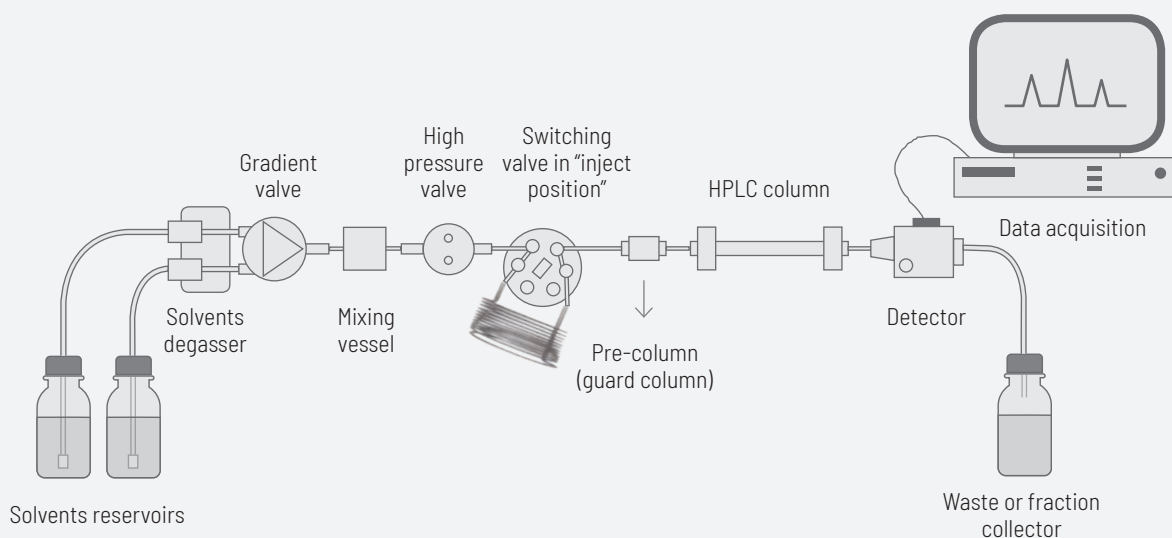


Apparatus

The **apparatus** typically consists of:

- A **pumping** system to deliver the mobile phase at a controlled flow rate.
 - The **mobile phase** is supplied from one or several reservoirs and flows through the column, usually at a constant rate, and then through the detector.
 - Solvents for the preparation of the mobile phase are normally free of stabilisers and, if an ultraviolet detector is employed, are transparent at the wavelength of detection. Solvents and other components employed are to be of appropriate quality.
 - The composition of the mobile phase may be kept constant ("**isocratic** elution mode") or varied ("**gradient** elution mode") during the chromatographic analysis.
- An **injector** to introduce the sample solution into the flowing mobile phase at or near the head of the column.
- A **chromatographic column** where the separation of the different species is performed. Most HPLC instruments also have a column oven that allows for adjusting the temperature at which the separation is performed.
- A **detector** that generates a signal proportional to the amount of sample component emerging from the column, hence allowing for quantitative analysis of the sample components. Various detectors are commonly used, such as ultraviolet/visible (UV/Vis) spectrophotometers, photodiode array (PDA) or mass spectrometers (MS).
- A **data acquisition system** or an integrator or a chart recorder that controls the HPLC instrument and provides data analysis.

Schematic representation of an HPLC unit



We offer a range of **solvents for HPLC and spectroscopy** specifically designed to be used in modern methods of instrumental analysis, as multipurpose solvents.

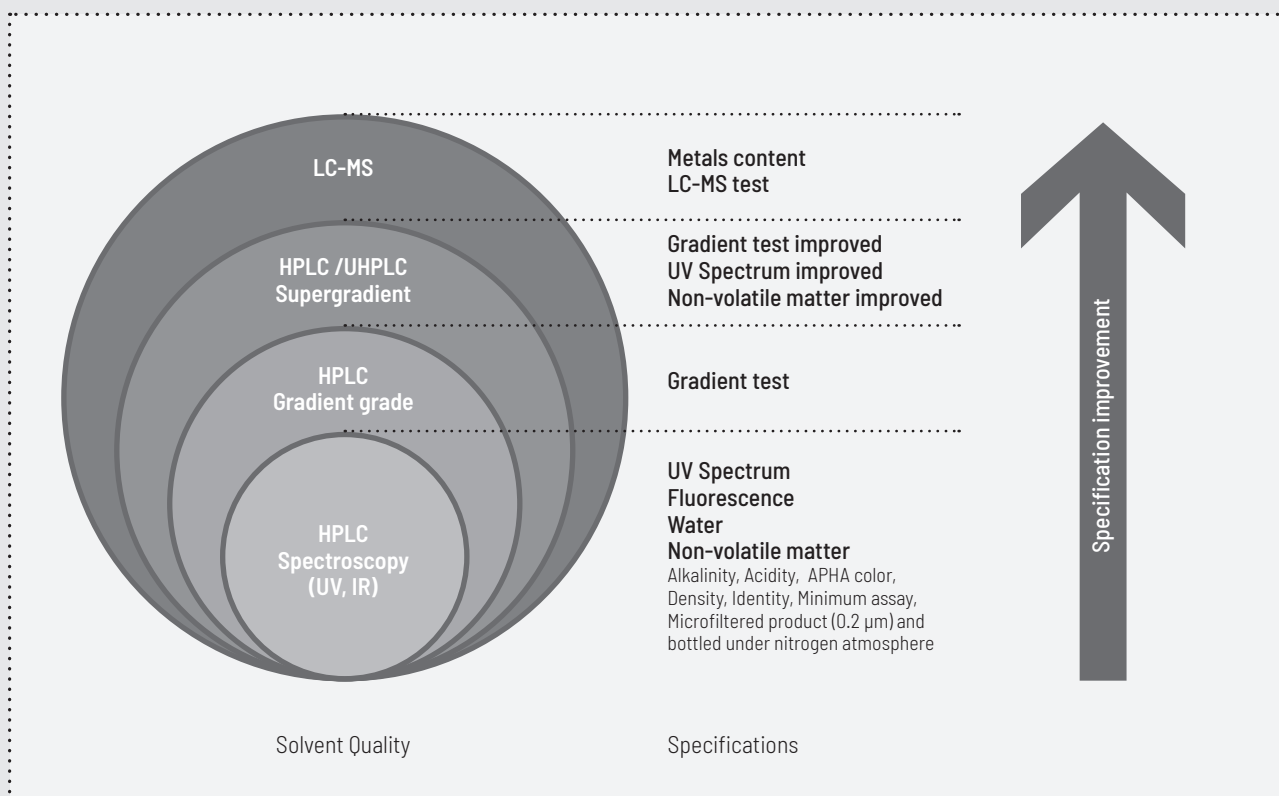
These products are **strictly controlled** in our analytical laboratory. Our quality control includes the following parameters that are very important in HPLC:

- the **IR spectrum** to confirm suitability for IR spectroscopy
- the **ultraviolet spectrum** to confirm the level of quality (high transmittance) required in HPLC and UV spectroscopy applications
- a **high assay level** (most solvents are 99.9%)
- a very **low level of evaporation residue** and water content

In addition, all these solvents are:

- **microfiltered** (0.2 microns) to guarantee the minimum level of particles
- **bottled under nitrogen** atmosphere, in order to maintain an optimum quality during storage and for a better conservation

Solvents of different quality are available depending on the final application and the type of equipment of chromatography and detector used:



We also offer other components that can be added to mobile phase as:

- **pH phase modifiers** used to influence the charge state of ionizable species in solution. The extent of analyte ionization can be used to affect retention and selectivity
- **Counter-ion** for ion-pair chromatography to control retention and reproducibility



Solvents for HPLC and Spectroscopy (UV, IR)

Product name	Code	Package
Acetone for UV, IR, HPLC, GPC, ACS	361007.1611	1000 ml
	361007.1612	2.5 L
	361007.16153	4 L
	361007.0515	10 L
	361007.0537	30 L
Acetonitrile for UV, IR, HPLC, ACS	361881.1611	1000 ml
	361881.1612	2.5 L
	361881.16153	4 L
	361881.0314	5 L
	361881.0516	25 L
Acetonitrile with 0.1% (v/v) of trifluoroacetic acid for HPLC	367170.0537	30 L
Benzene for UV, IR, HPLC, GPC, ACS	361192.1611	1000 ml
1-Butanol for UV, IR, HPLC	361082.1611	1000 ml
tert-Butyl Methyl Ether for UV, IR, HPLC	363312.1611	1000 ml
	363312.1612	2.5 L
Carbon Disulfide for UV, IR, HPLC	361244.1611	1000 ml
Chloroform stabilized with ~ 150 ppm of amylene for HPLC, GPC	363101.1612	2.5 L
Chloroform stabilized with ethanol for UV, IR, HPLC	361252.1611	1000 ml
	361252.1612	2.5 L
Cyclohexane for UV, IR, HPLC, ACS	361250.1611	1000 ml
	361250.1612	2.5 L
	361250.0515	10 L
	361250.0537	30 L
Dichloromethane stabilized with ~ 20 ppm of amylene for UV, IR, HPLC, GPC, ACS	361254.1611	1000 ml
	361254.1612	2.5 L
	361254.16153	4 L
	361254.0516	25 L
Diethyl Ether stabilized with ethanol for UV, IR, HPLC	362551.1611	1000 ml
	362551.0537	30 L
N,N-Dimethylacetamide for UV, IR, HPLC	363145.1611	1000 ml
	363145.1612	2.5 L
N,N-Dimethylformamide for UV, IR, HPLC, GPC, ACS	361785.1611	1000 ml
	361785.1612	2.5 L
Dimethyl Sulfoxide for UV, IR, HPLC, GPC	361954.1611	1000 ml
	361954.1612	2.5 L
Ethanol absolute for UV, IR, HPLC	361086.1611	1000 ml
	361086.1612	2.5 L
	361086.16153	4 L
Ethanol 96% v/v for UV, IR, HPLC	361085.1611	1000 ml
	361085.0537	30 L

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Product name	Code	Package
Ethyl Acetate for UV, IR, HPLC, ACS	361318.1611	1000 ml
	361318.1612	2.5 L
	361318.16153	4 L
	361318.0515	10 L
n-Heptane for UV, IR, HPLC	362062.1611	1000 ml
	362062.1612	2.5 L
	362062.0314	5 L
	362062.0537	30 L
n-Heptane for UV, IR, HPLC	362063.1611	1000 ml
	362063.1612	2.5 L
	362063.16153	4 L
n-Hexane 95% for UV, IR, HPLC, ACS	363242.1611	1000 ml
	363242.1612	2.5 L
	363242.0515	10 L
	363242.0537	30 L
Hexane, alkanes mixture for HPLC	361347.1612	2.5 L
Isooctane for UV, IR, HPLC, ACS	362064.1611	1000 ml
	362064.1612	2.5 L
	362064.16153	4 L
Methanol for UV, IR, HPLC, ACS	361091.1611	1000 ml
	361091.1612	2.5 L
	361091.16153	4 L
n-Pentane for UV, IR, HPLC	362006.1611	1000 ml
	362006.1612	2.5 L
1-Propanol for UV, IR, HPLC	361885.1611	1000 ml
	361885.1612	2.5 L
2-Propanol for HPLC	361090.1611	1000 ml
	361090.1612	2.5 L
	361090.16153	4 L
Propionitrile for UV, HPLC	365732.1611	1000 ml
Tetrachloroethylene for UV, IR, HPLC, GPC	361455.1611	1000 ml
	361455.1612	2.5 L
Tetrahydrofuran for UV, IR, HPLC, GPC	361736.1611	1000 ml
	361736.1612	2.5 L
Toluene for UV, IR, HPLC, GPC, ACS	361745.1611	1000 ml
	361745.1612	2.5 L
	361745.16153	4 L
1,2,4-Trichlorobenzene for UV, IR, HPLC, GPC	363541.1612	2.5 L
Water for UV, HPLC, ACS	361074.1611	1000 ml
	361074.1612	2.5 L
Water with 0.1% (v/v) of trifluoroacetic acid for HPLC	367171.0537	30 L



Reagents for IR Spectroscopy

Product name	Code	Package
Potassium Bromide for IR	331489.1608	100 g
	331489.1609	250 g
Tetrachloroethylene for IR	331455.1612	2.5 L



Solvents for LC-MS

Product name	Code	Package
Acetonitrile for LC-MS	701881.1611	1000 ml
	701881.1612	2.5 L
Methanol for LC-MS	701091.1611	1000 ml
	701091.1612	2.5 L
Water for LC-MS	701074.1611	1000 ml
	701074.1612	2.5 L
Water with 0.1% formic acid LC-MS grade	707187.1612	2.5 L

pH mobile phase modifiers

Product name	Code	Package
Acetic Acid glacial for HPLC	361008.1611	1000 ml
	361008.1612	2.5 L
	363317.1606	25 ml
Trifluoroacetic Acid for UV	363317.1608	100 ml
	363317.1609	250 ml

Solvents for HPLC/UHPLC gradient

Product name	Code	Package
Acetonitrile for UHPLC Supergradient, ACS	221881.1611	1000 ml
	221881.1612	2.5 L
	221881.16153	4 L
	221881.0314	5 L
	221881.0515	10 L
	221881.0516	25 L
	221881.0537	30 L
	221881.0519	200 L
Ethanol absolute for HPLC gradient	221086.1611	1000 ml
	221086.1612	2.5 L
Methanol for UHPLC Supergradient, ACS	221091.1611	1000 ml
	221091.1612	2.5 L
	221091.16153	4 L
	221091.0314	5 L
	221091.0515	10 L
	221091.0516	25 L
	221091.0537	30 L
	221091.0519	200 L
2-Propanol for HPLC gradient	221090.1611	1000 ml
	221090.1612	2.5 L
Water for UHPLC Supergradient	221074.1611	1000 ml
	221074.1612	2.5 L





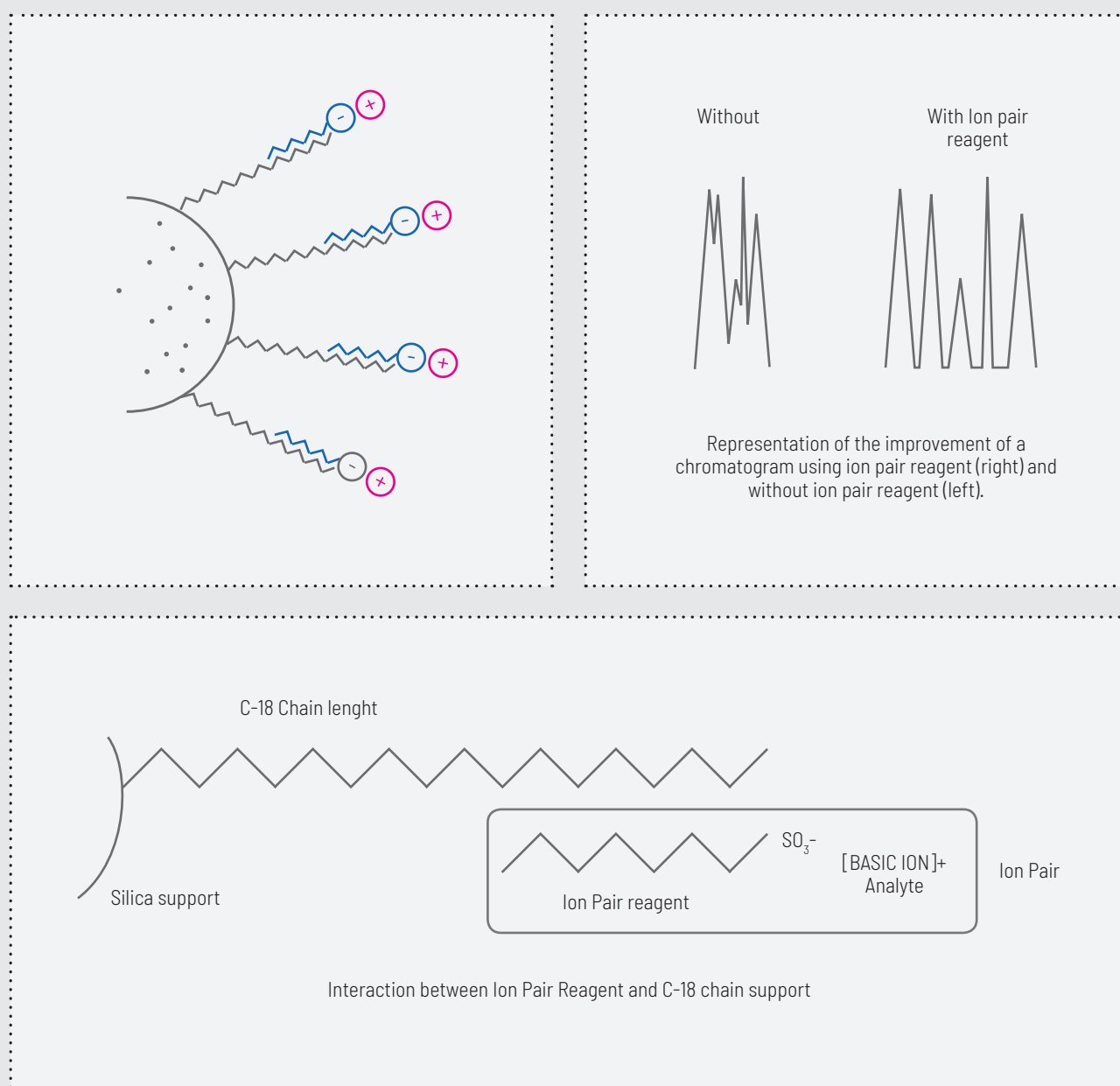
Ion pairing reagents

Ion Pair Chromatography is used **to separate ionic analytes on a reversed phase column in HPLC**. This chromatography is based on the **addition of ionic compounds** (ion pair reagents) to the mobile phase to promote the formation of ion pairs with ionic analytes in the sample to modulate retention of the ionic analytes.

The increase in hydrophobic character of the ion pair (electrically neutral) results in a greater affinity for the reverse stationary phase and leads to an increase in sample resolution.

UV detectors are widely used. Therefore ion-pair reagents must lack UV absorption themselves to obtain highly sensitive detection of samples. The UV absorption of sodium alkanesulfonates and quaternary ammonium salts is minimal so that these reagents can be used for reliable HPLC analysis.

The purity of mobile phase additives is of utmost importance to their successful application.

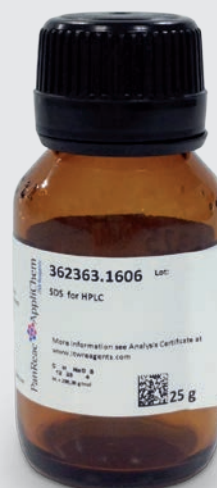


In a regular reversed-phase chromatography system, the analyte is incapable of making significant interactions with the non-polar surface of the stationary phase and hence elutes out immediately without much retention with little or no resolution observed.

In reversed-phase ion-pairing chromatography the analyte is present in a mobile phase containing a suitable ion-pairing agent. The agent forms an ion-pair via ionic interactions with the analyte to make it more non-polar. As a result the analyte gets more retained on the stationary phase and elutes out more gradually.

All our Ion Pair reagents are rigorously controlled with special emphasis on the requirements of modern reversed phase HPLC:

- High purity
- UV and IR transparency



Product name	Assay (min.)	Code	Package
1-Butane Sulfonic Acid Sodium Salt for HPLC	99.0 % *	365769.1606	25 g
1-Decanesulfonic Acid Sodium Salt for HPLC	99 %	367127.1606	25 g
1-Heptane Sulfonic Acid Sodium Salt for HPLC	99.0 % *	364897.1606	25 g
1-Heptane Sulfonic Acid Sodium Salt 1-hydrate for HPLC	99 %	367128.1606	25 g
1-Hexane Sulfonic Acid Sodium Salt for HPLC	99.0 % *	363428.1606	25 g
1-Hexane Sulfonic Acid Sodium Salt 1-hydrate for HPLC	99 %	367129.1606	25 g
1-Octane Sulfonic Acid Sodium Salt for HPLC	99.0 % *	363995.1605	10 g
		363995.1606	25 g
1-Pentane Sulfonic Acid Sodium Salt for HPLC	99.0 % *	364896.1606	25 g
SDS for HPLC	99.0 %	362363.1606	25 g
Tetrabutylammonium di-Hydrogen Phosphate for HPLC	99 % *	367038.1606	25 g
Tetrabutylammonium Hydrogen Sulfate for HPLC	99 %	363622.1606	25 g
		363622.1607	50 g
		363622.1610	500 g

* as dried substance



Gas Chromatography

In **Gas Chromatography** (GC) the mobile phase is a carrier gas moving through or passing the stationary phase contained in a column.

It is applicable to substances or their derivatives which are volatilized under the temperatures employed.

GC is based on mechanisms of adsorption, mass distribution or size exclusion.



Apparatus

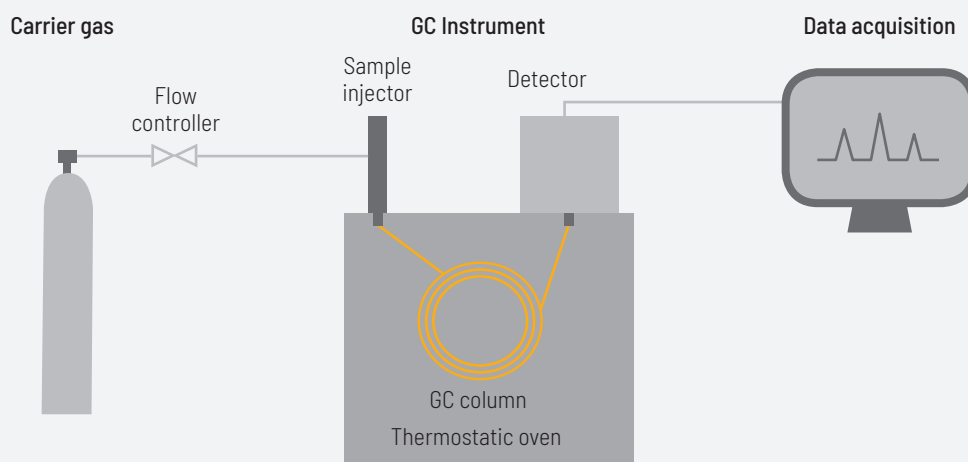
The **apparatus** consists of:

- **Injector**
- Chromatographic **column** contained in an oven
- **Detector**
- **Data acquisition** system (or an integrator or a chart recorder)

The carrier gas flows through the columns at a controlled rate or pressure and then through the detector.

The chromatography is carried out either at a constant temperature or according to a given temperature programme.

Schematic representation of an GC unit

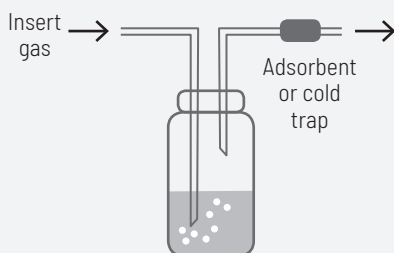


Injectors

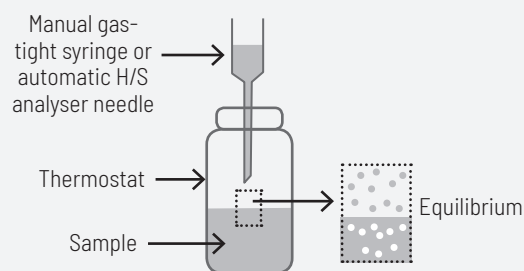
Direct injections of solutions are the usual mode of injection, unless otherwise prescribed in the monograph. Injection may be carried out either directly at the head of the column using a syringe or an injection valve, or into a vaporization chamber which may be equipped with a stream splitter.

Injectations of vapor phase may be effected by static or dynamic head-space injection systems:

Dynamic head-space (purge and trap) injection systems include a sparging device by which volatile substances in solution are swept into an adsorbent column maintained at a low temperature. Retained substances are then desorbed into the mobile phase by rapid heating of the adsorbent column.



Static head-space injection systems include a thermostatically controlled sample heating chamber in which closed vials containing solid or liquid samples are placed for a fixed period of time to allow the volatile components of the sample to reach equilibrium between the non-gaseous phase and the vapor phase. After equilibrium has been established, a predetermined amount of the head-space of the vial is flushed into the gas chromatograph.



Stationary phases

Stationary phases are contained in columns which may be:

- A capillary column of fused-silica whose wall is coated with the stationary phase.
- A column packed with inert particles impregnated with the stationary phase.
- A column packed with solid stationary phase.

Capillary columns are 0.1 mm to 0.53 mm in the internal diameter and 5 m to 60 m in length. The liquid or stationary phase, which may be chemically bonded to the inner surface, is a film 0.1 μm to 5.0 μm thick.

Packed columns, made of glass or metal, are usually 1 m to 3 m in length with an internal diameter of 2 mm to 4 mm. Stationary phases usually consist of porous polymers or solid supports impregnated with liquid phase.

Mobile phases

Helium or nitrogen are usually employed as the carrier gas for packed columns, whereas commonly used carrier gases for capillary columns are nitrogen, helium and hydrogen.

Detectors

Flame-ionization detectors (FID) are usually employed but additional detectors such as nitrogen-phosphorus (NPD), mass spectrometric (MSD), thermal conductivity (TCD) and others may be used, depending on the purpose of the analysis.

Reagents for Pharma Industry

Chapter 4



We offer a range of solvents for GC specifically designed for use in modern methods of instrumental analysis. These products are strictly controlled in our analytical laboratory by gas chromatography. We distinguish two different qualities depending on the final purpose of analysis:

Solvents for GC, ECD and FID

This range of high purity solvents has been specifically designed for the analysis of pesticide residues in the food industry and in environmental control, for example in drinking water.

The analysis is performed on a 500-fold concentrated sample. The sample is then injected into the gas chromatograph using the ECD and the FID detectors.

- Using an ECD detector in the interval from lindane to DDT (there are no peaks greater than 5 ng/l of lindane).
- Using a FID detector in the interval from 2-octanol to tetradecanol.

These solvents are carefully packaged and the liquid only comes into contact with glass and teflon.

Solvents for Headspace GC-MS

These solvents are specially purified to be used in the preparation of samples of actives, excipients and medicines to determine residual solvents by headspace gas chromatography.

- The concentrations typically found of residual solvents in our GC-Headspace grade solvents are less than 0.5 ppm for class 1, less than 5 ppm for class 2 and less than 25 ppm for class 3.

These solvents are carefully packaged and the liquid only comes into contact with glass and teflon.

To ensure the highest quality of these solvents it has been necessary to develop new and more demanding manufacturing and packaging protocols.

In addition, we offer some **GC derivatization reagents** for silylation.

In gas chromatography, some compounds have to be derivatized, mainly those containing polar functional groups (active hydrogens), in order to improve their volatility, thermal stability and, in some cases, detection sensitivity. For example, halogen atoms (trifluoroacetates) can be introduced to increase the detection limit when using electron capture detectors (ECDs).

All reagents are supplied in 1 ml and 10 ml vials with teflon septum.



Solvents and reagents for GC, ECD and FID

Product name	Code	Package
Acetone	321007.1611	1000 ml
	321007.1612	2.5 L
	321007.16153	4 L
	321007.0516	25 L
Acetonitrile	321881.1612	2.5 L
Chloroform stabilized with ethanol	321252.1612	2.5 L
Cyclohexane	321250.1611	1000 ml
	321250.1612	2.5 L
	321250.16153	4 L
Mixture Cyclohexane/Ethyl Acetate 1:1 v/v	326165.0516	25 L
Dichloromethane stabilized with ~ 20 ppm of amylene	321254.1611	1000 ml
	321254.1612	2.5 L
	321254.16153	4 L
Diethyl Ether stabilized with ethanol	322551.1611	1000 ml
Ethyl Acetate	321318.1611	1000 ml
	321318.1612	2.5 L
	321318.16153	4 L
	321318.0515	10 L
n-Heptane	322062.1612	2.5 L
n-Hexane 95%	323242.1611	1000 ml
	323242.1612	2.5 L
	323242.16153	4 L
	323242.0515	10 L
	323242.0516	25 L
	323242.0537	30 L
Hexane, alkanes mixture	321347.0316	25 L
Isooctane	322064.1611	1000 ml
	322064.1612	2.5 L
Methanol	321091.1611	1000 ml
	321091.1612	2.5 L
n-Pentane	322006.1612	2.5 L
Petroleum Ether 40-60°C	321315.1611	1000 ml
	321315.1612	2.5 L
	321315.0515	10 L
2-Propanol	321090.1611	1000 ml
Sodium Sulfate anhydrous, granulated	325708.1611	1000 g
Sodium Sulfate anhydrous, powder	325709.1611	1000 g
Toluene	321745.1611	1000 ml
	321745.1612	2.5 L



Solvents for Headspace GC-MS













Product name	Code	Package
N,N-Dimethylacetamide for Headspace GC	753145.1611	1000 ml
	753145.1612	2.5 L
N,N-Dimethylformamide for Headspace GC	751785.1611	1000 ml
	751785.1612	2.5 L
Dimethyl Sulfoxide for Headspace GC	751954.1611	1000 ml
	751954.1612	2.5 L

Derivatization reagents for GC

Product name	Code	Package
Bis-(Trimethylsilyl)-Trifluoroacetamide for GC	355588.1905	10 ml
	355588.1606	25 ml
N-Methyl-N-(Trimethylsilyl)-Trifluoroacetamide for GC	355587.1604	5 ml
	355587.2522	10 x 10 ml
Silan-Sterol-1 for GC	355650.0922	20 x 1 ml



Package pictograms

	Glass bottle		Aluminium bottle
	Plastic bottle		Aluminium bottle with outer packaging
	Plastic jerrycan		Tin-plated can
	Stainless steel drum (returnable)		Co-extrusion bottle (multilayer)
	Sol-Pack: Plastic container in a carton box (cubitainer), with tap		Glass ampoule
	Steel-plated drum		Crimp top vial with septum



A195-4,EN:201809



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