Ion chromatography – the all-rounder for pharmaceutical analysis

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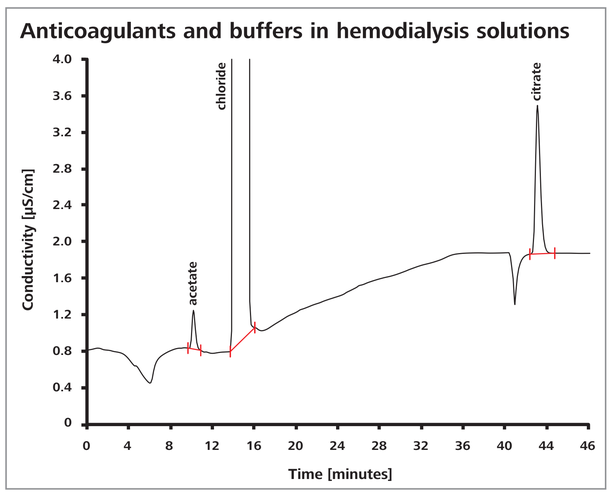
Pharmaceutical solutions

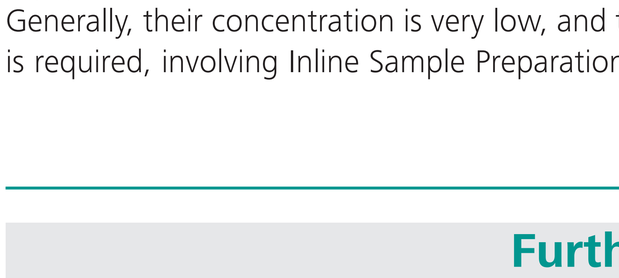
Pharmaceutical solutions denote isotonic, hemodialysis, or infusion solutions, containing ingredients in concentrations of several orders of magnitude. IC accomplishes their analyses precisely and with short running times. Thereby, intelligent analytical procedures and Inline Sample Preparation (MISP), e.g., Matrix Elimination (ME) or Preconcentration (MiPCT), imply minimal efforts.

Anticoagulants and buffers in hemodialysis solutions



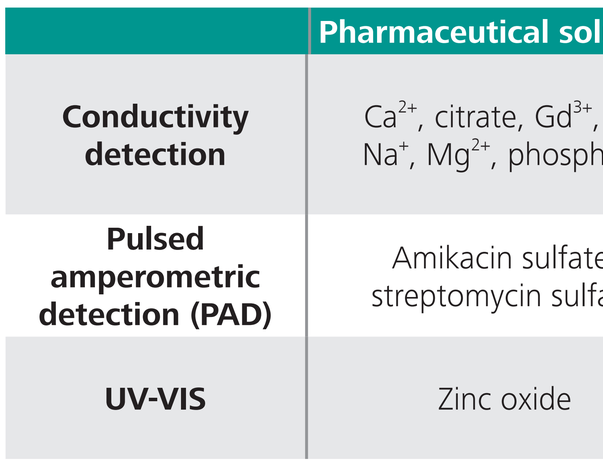
Acetate and citrate in diluted hemodialysis solution measured on a Metrosep A Supp 7 - 250/4.0 using a Na_2CO_3-gradient and conductivity detection after sequential suppression.

Metrohm intelligent Preconcentration Technique (MiPCT)



Impurities

Precurser residues in antihypertensive drugs



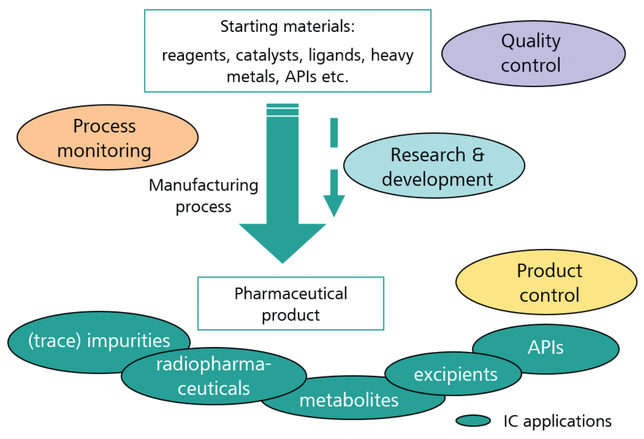
Irbesartan sample spiked with 5–80 µg/L azide; column: Metrosep A Supp 10 - 250/4.0; eluent: 5 mmol/L Na_2CO_3 and 5 mmol/L $NaHCO_3$; Inline Matrix Elimination (ME) with 70:30 (v/v) methanol/water and followed by suppressed conductivity detection.

Impurities are mainly introduced from the starting materials used and/or during synthesis of the APIs. They are monitored according to the pharmacopeias. Generally, their concentration is very low, and therefore analysis at trace levels is required, involving Inline Sample Preparation (MISP).

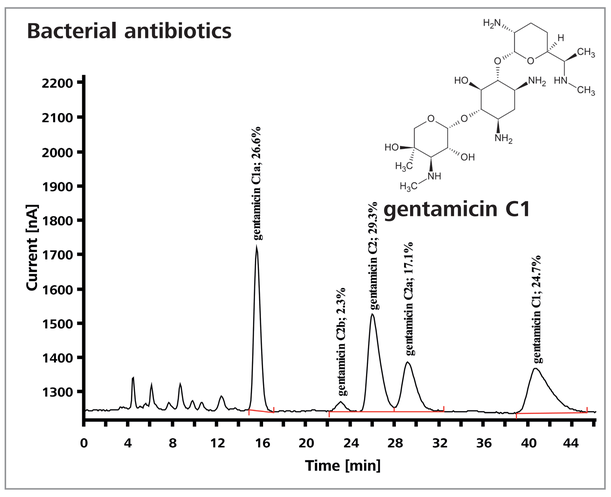
Active pharmaceutical ingredients (APIs)

APIs are used to cure, alleviate, prevent, or identify illnesses and diseases. They are present in small quantities and aim at restoring physiological functions in human beings. Prominent examples are gentamicin, neomycin, and cefadroxil. With IC, these ingredients can be accurately determined in accordance with the US Pharmacopeia (USP) and the European Pharmacopoeia (Ph. Eur.).

Production of pharmaceuticals



Bacterial antibiotics



Separation of gentamicin analogs on a RP-S column (Polymer Laboratories) applying post-column addition of 300 mmol/L NaOH with pulsed amperometric detection (PAD).

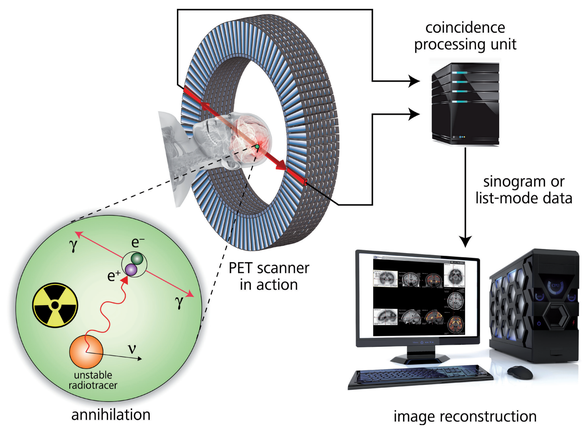
IC – a pharmaceutical standard method

Pharmaceutical analysis guarantees drug safety by providing information on the identity, content, quality, purity, and stability of pharmaceutical products using analytical chemistry. Ion chromatography (IC) offers a broad range of pharmacopeia-compliant applications for quality control, monitoring, and improving drug manufacturing.

As a very accurate and versatile technique, IC meets the requirements of many pharmaceutical applications. IC is a USP-accepted standard method for the determination of active pharmaceutical ingredients (APIs), excipients, impurities, pharmaceutical solutions as well as pharmaceutical starting materials, finished pharmaceutical products (FPPs) and even body fluids.

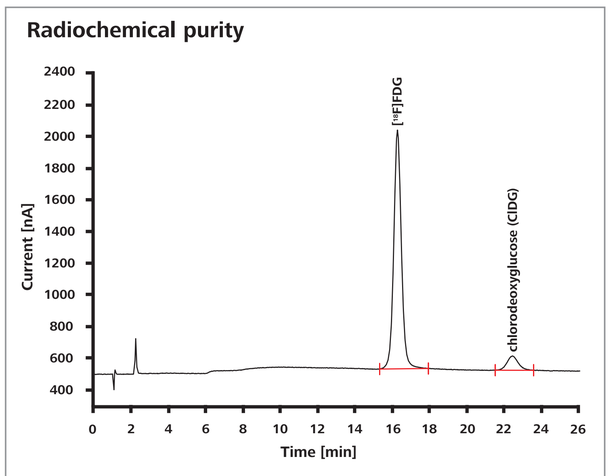
IC supports the analysis of several substances within a very short time and in a single analysis distinguishing chemically similar analytes in mg/L to even µg/L levels. Thereby, interferences caused by the sample matrix can be efficiently eliminated by specific Inline Sample Preparation (MISP) tools and the use of appropriate detection methods (see table below).

Positron emission tomography



Radio IC

Radiochemical purity



Chromatogram with peaks of the radiotracer [^{18}F]FDG and the impurity chlorodeoxyglucose analyzed on a Metrosep Carb 2 - 150/4.0 using 0.1 mol/L NaOH and pulsed amperometric detection (PAD).

Radiopharmaceuticals are radioactive substances used for 3D-imaging in nuclear medicine to study biochemical and physiological processes. [^{18}F]Fluordeoxyglucose ([^{18}F]FDG) is commonly used as radiopharmaceutical in positron emission tomography (PET), e.g., to explore cancer metastasis or brain mapping. Radio IC is a flexible and safe high-performance method to control the purity of radiochemicals.

Further applications for pharmaceutical use of IC

	Pharmaceutical solutions	APIs/antibiotics	Impurities
Conductivity detection	Ca^{2+}, citrate, Gd^{3+}, K^+, Na^+, Mg^{2+}, phosphate	Bethanechol, binding capacity of phosphate, camphorsulfonic acid, dicyclopropylmethylamine, ibandronate, K^+, N-methyl-D-glucamine (meglumine), piperazine, Zn^{2+}	Amines, azide, bromide, Ca^{2+}, diethyl sulfate, dimethyl sulfate, EDTA, hydrazine, K^+, Li^+, Mg^{2+}, monomethyl-/dimethylamine, Na^+, N-methylpyrrolidine, Rb^+, tetrabutylammonium
Pulsed amperometric detection (PAD)	Amikacin sulfate, streptomycin sulfate	Adrenaline, ß-cyclodextrin, ephedrine, gentamicin, kanamycin sulfate, neomycin, norephedrine, pseudoephedrine, ribitol	Cyanide, propargyl alcohol, propylene glycol
UV-VIS	Zinc oxide	Amoxicillin, cefadroxil, ibuprofen, paracetamol, ranitidine hydrochloride, theophylline, thiamine hydrochloride, valerophenone, vitamin C	EDTA, salicylic acid, valerophenone

References: - **Ion chromatography – the all-rounder in pharmaceutical analysis** (WP-019EN), Metrohm: Herisau, Switzerland, 2017; p 6.
- **Pharmaceutical analysis** (8.000.5139EN); Metrohm: Herisau, Switzerland, 2015; p 28.

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