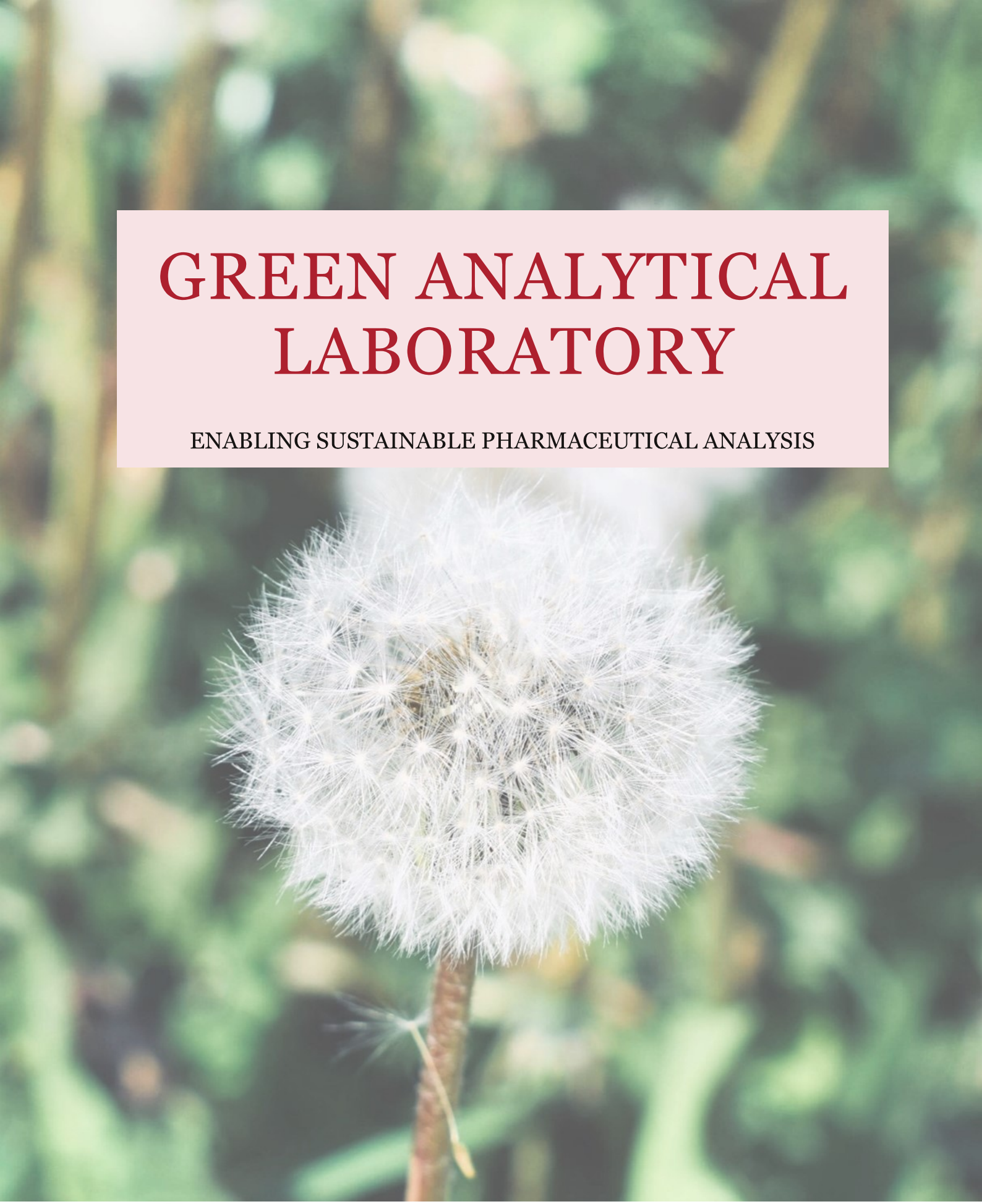


GREEN ANALYTICAL LABORATORY

ENABLING SUSTAINABLE PHARMACEUTICAL ANALYSIS

ELECTROKINETIC SEPARATIONS
RESEARCH GROUP

INTRODUCTION

prof. RNDr. Marián Masár, PhD.
Head of Department
Analytical Chemistry

The pharmaceutical industry, as well as other industries, are committed to achieving the so-called "Net Zero initiative" [1], where the amount of CO_2 released into the atmosphere is balanced with the amount of CO_2 collected from the atmosphere. This also includes indirect emissions, e.g., emissions associated with the treatment of chemical waste. The "Net Zero" objectives can be achieved in several ways, including through chemical synthesis meeting the principles of green chemistry [2,3], reducing the environmental impact of pharmaceuticals and other bio-active substances and, last but not least, focusing on emission control. The last category includes activities aimed at reducing harmful waste, reducing water and energy consumption and focusing on renewable energy sources. These activities, which are in line with the "UN Race to Zero Campaign [4]", create new challenges for pharmaceutical analysis. Sample preparation and analysis itself currently rely on the use of organic solvents. This adverse impact on the environment can be significantly reduced or completely eliminated, thereby contributing to the objectives of "Net Zero" by applying so-called miniaturized instrumental methods. Miniaturized separation techniques, which include capillary and microchip electrophoresis (CE and MCE), are based on the principle of electro-kinetic phenomena, where analytes are separated from each other based on differences in ion mobility. From the point of view of green analytical chemistry [4,5], these techniques offer several potential advantages over conventional analytical approaches: (i) very low consumption of working solutions, (ii) virtually complete elimination of organic solvents in working solutions and sample preparation, (iii) reduced energy consumption for analysis due to faster analysis and response of such devices. One of the disadvantages of miniaturized analytical systems is the lower concentration sensitivity compared to conventional systems, especially when using the so-called "on-column" detection. Recent developments in the miniaturisation of ion mobility spectrometry (IMS) [6] have made it possible to successfully combine this detection and identification technique with the above-mentioned miniaturised separation systems. According to the available literature [7], this technique provides sufficient sensitivity for the determination of impurities in pharmaceutically active compounds complying with international recommendations.

References

1. U.S. Launches Net-Zero World Initiative to Accelerate Global Energy System Decarbonization, Department of Energy, https://www.energy.gov (accessed on 7 November 2022).
2. Koel M., Kaljurand M., Pure Appl. Chem. 78 (2006) 1993.
3. Anastas P.T., Warner J.C., Green Chemistry: Theory and Practice, Oxford University Press, New York, 1998.
4. Namiesnik J., Environ. Sci. Pollut. Res. 6 (1999) 243.
5. Anastas P.T., Crit. Rev. Anal. Chem. 29 (1999) 167.
6. Masár M., Hradski J., Nováková M., Szucs R., Sabo M., Matejčík S., Sens. Actuators B Chem. 302 (2020) 127183.
7. O'Donnell R.M., Sun X., Harrington P.D.B., TrAC-Trends Anal. Chem. 27 (2008) 44.

Comenius University Bratislava

Comenius University Bratislava is modern European university which was established in 1919. It is build on a solid foundation of academic traditions. It is the largest and most prominent university in Slovakia. Comenius University regularly appears in global rankings of the world's top universities, typically ranks among top 3% (CWUR). It consists of 13 faculties and offers more than 700 study programs. In addition to teaching Comenius University is a research institution which supports hundreds of domestic and international science and research projects.

Faculty of Natural Sciences

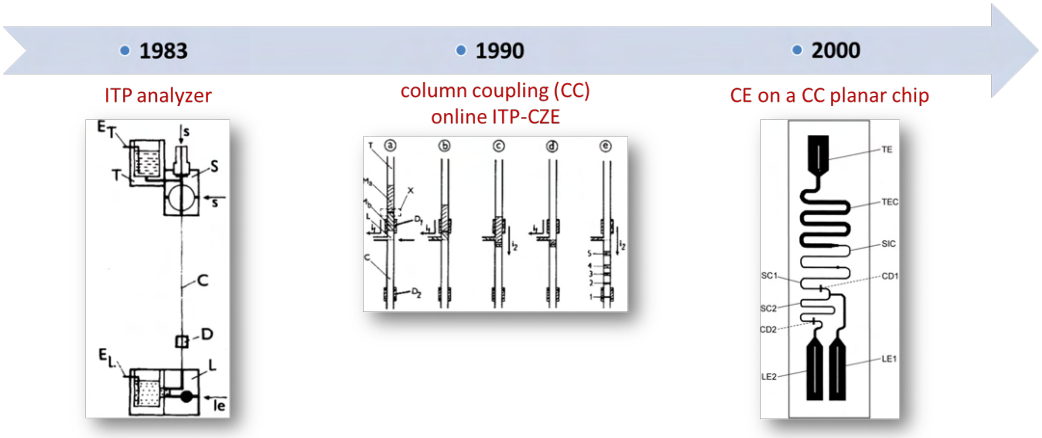
Faculty of Natural sciences was established 1940. It resides on modern, purpose-built campus (1967 – 1988) which has recently undergone extensive refurbishments of teaching as well laboratory facilities. There are six scientific sections belong to the faculty, namely Biology, Chemistry, Environmental studies, Geology and Geography. Faculty of Natural Sciences supports thriving network of national and international research collaborations.

For more information
https://uniba.sk/fileadmin/ruk/ovv/2022/Dokumenty/2022_UK_v_Grafoch_a_cislach_EN_WEB.pdf

Department of Analytical Chemistry
Electrokinetic Separations Research Group

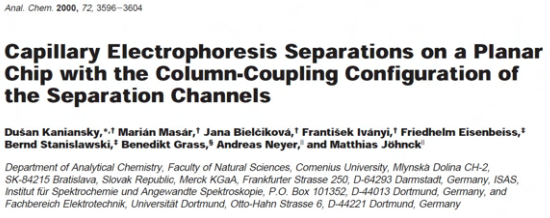
History

The Department of Analytical Chemistry at Comenius University Bratislava was established in 1955 and is the oldest analytical chemistry department in Slovakia. The department was initially led by prof. Stankoviansky, co-founder of electrochemistry in Slovakia. The Laboratory of Separation Methods was established in 1968. The founder of the Slovak scientific school in the field of electrokinetic separation techniques was Prof. Dušan Kaniansky. His research was focused on the development of electrophoretic analyzers and multidimensional electrokinetic separations and (ultra)trace analysis of multicomponent mixtures of substances on the capillaries and microchips. The work of Prof. Kaniansky and his coworkers, which introduced a coupling of capillary isotachophoresis with radiometric and amperometric detection as well as mass spectrometry, holds a significant position in the early developments of capillary electrophoresis.



Most important contributions

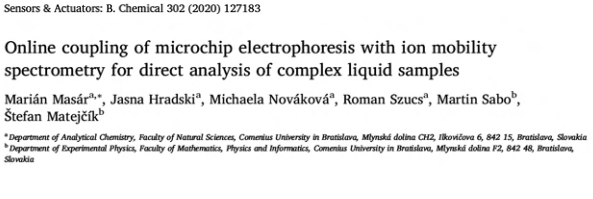
- Significant contribution to the development of the fundamentals of electrokinetic separation techniques
- First PMMA chip for Electrophoresis with coupled channels, integration of sample preparation, separation and detection, or also post-chip sample handling in lab-on-a-chip context
- Combination of various modes of electrokinetic separations (CE-CE, ITP-CE)
- Improvement of detection sensitivity in Hydrodynamically closed system and design of commercial instrumentation.


Anal. Chem. 2000, 72, 3596–3604

Capillary Electrophoresis Separations on a Planar Chip with the Column-Coupling Configuration of the Separation Channels

Dušan Kaniansky,*,† Marián Masár,† Jana Bielčíková,† František Iványi,† Friedhelm Eisenbeiss,‡ Bernd Stanislawski,‡ Benedikt Grass,§ Andreas Neyer,§ and Matthias Jöhnck§

Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University, Mlynská Dolina CH-2, SK-84215 Bratislava, Slovak Republic, Merck KGaA, Frankfurter Strasse 250, D-64293 Darmstadt, Germany, ISAS, Institut für Spektrochemie und Angewandte Spektroskopie, P.O. Box 101352, D-44013 Dortmund, Germany, and Fachbereich Elektrotechnik, Universität Dortmund, Otto-Hahn Strasse 6, D-44221 Dortmund, Germany


Sensors & Actuators: B. Chemical 302 (2020) 127183

Online coupling of microchip electrophoresis with ion mobility spectrometry for direct analysis of complex liquid samples

Marián Masár[a,*], Jasna Hradski[a], Michaela Nováková[a], Roman Szucs[a], Martin Sabo[b], Štefan Matejčík[b]

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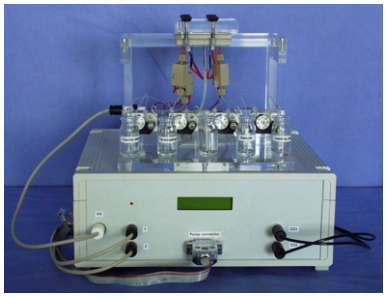
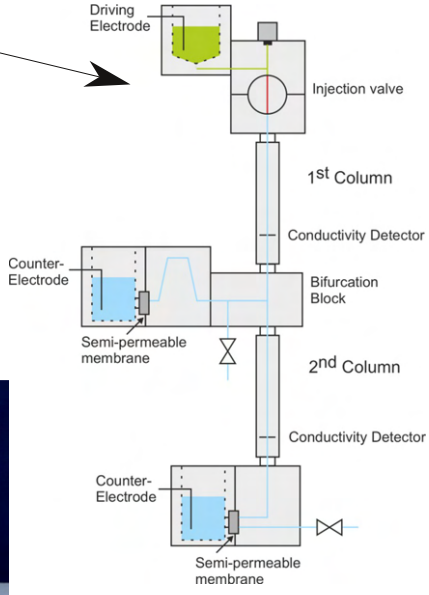
Electrokinetic Separations Research Group

Access to Technology and Benefits

Microchip Electrophoresis
Integration of elements of Analytical test procedure on single chip (LOTC)



CE in Hydrodynamically closed system
approx. 20-fold improvement of detection sensitivity



Capillary Electrophoresis
Coupling of multiple separation (CE-CE, ITP-CE) and detection techniques (UV, Conductivity, MS)

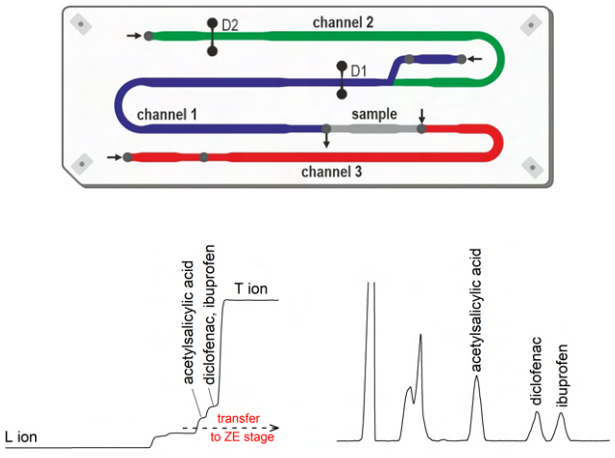
Most important publications

- Marián Masár, Jasna Hradski, Martin G. Schmid, Roman Szucs. *Advantages and pitfalls of capillary electrophoresis of pharmaceutical compounds and their enantiomers in complex samples: Comparison of hydrodynamically opened and closed systems*. Int. J. Mol. Sci. 21 (2020) 6852.
- Peter Troška, Jasna Hradski, Lucia Chropeňová, Roman Szucs, Marián Masár. *Potential of microchip electrophoresis in pharmaceutical analysis: Development of a universal method for frequently prescribed nonsteroidal anti-inflammatory drugs*. J. Chromatogr. A 1654 (2021) 462453.
- Jasna Hradski, Mária Drusková Chorváthová, Róbert Bodor, Martin Sabo, Štefan Matejčík, Marián Masár. *Quantitative aspects of microchip isotachophoresis for high precision determination of main components in pharmaceuticals*. Anal. Bioanal. Chem. 408 (2016) 8669.
- Marián Masár, Peter Troška, Jasna Hradski, Ivan Talian. *Microchip isotachophoresis coupled to surface-enhanced Raman spectroscopy for pharmaceutical analysis*. Microchim. Acta 187 (2020) 448.
- Marián Masár, Jasna Hradski, Michaela Nováková, Roman Szucs, Martin Sabo, Štefan Matejčík. *Online coupling of microchip electrophoresis with ion mobility spectrometry for direct analysis of complex liquid samples*. Sens. Actuators B Chem. 302 (2020) 127183.

Analysis of Pharmaceutical and Bioactive compounds

Development of new miniaturized pre-treatment and concentration techniques for the analysis of pharmaceuticals and bio-active substances without the use of organic solvents

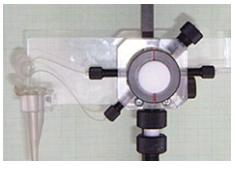
Most samples of pharmaceuticals and bio-active substances require some form of pre-treatment before analysis. In the simplest case, this process involves the dissolution of the analyte in a liquid compatible with the applied analytical technique. For example, in the case of conventional LC, these substances dissolve in solutions of organic solvents. In more complex cases, analytes are selectively extracted from a complex matrix, often in order to increase their concentration in the final solution. The aim of this research is to develop a method of preparing CE and MCE-compatible samples in which the use of organic solvents will be completely eliminated. This will be achieved by the addition of various additives, e.g. cyclodextrins, surfactants, ionic liquids, etc.

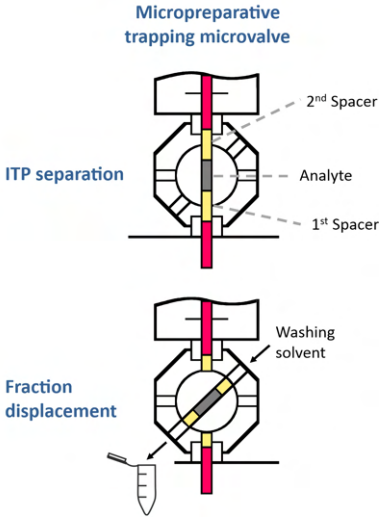


Troška P., Hradski J., Chropeňová L., Szucs R., Masár M., J. Chromatogr. A 1654 (2021) 462453.

Study and design of new environmentally sustainable ways of isolation and purification of pharmaceutical products and bio-active substances

Conventional preparative and purification approaches generate several times higher volumes of toxic waste compared to analytical techniques, as they use higher solvent flow rates and volumes and larger separation column dimensions. The aim of this part of the research is to confirm the hypothesis that selected analytes can be selectively isolated from a complex matrix also with the help of micropreparative isotachophoresis (mpITP). In this preparation technique, aqueous buffer solutions will be used exclusively, thereby significantly reducing the negative impact on the environment.

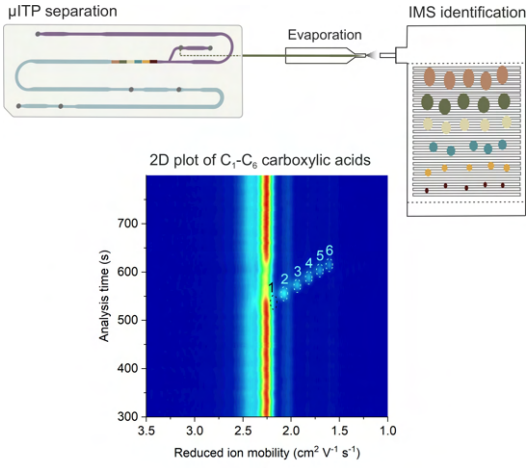




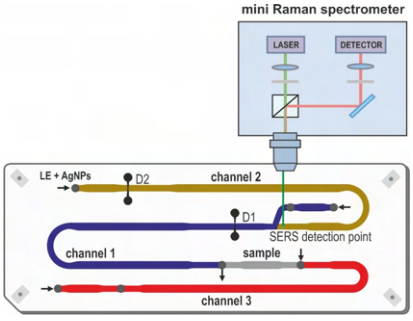
Analysis of Pharmaceutical and Bioactive compounds

Development of new, low-energy methods for identification of pharmaceuticals and bio-active substances

Analytical instruments designed to identify unknown substances are typically highly energy consuming and use compressed gases and operate under vacuum. The alternative, based on miniaturized IMS, operates at atmospheric pressure, without compressed gases. For complex multicomponent matrices, there is the possibility of combining this identification and detection technique with a separation technique such as MCE. This part of the research also requires the development of functional interfaces for the hyphenation of miniaturized separation and detection techniques for trace analysis of pharmaceuticals and bio-active substances.



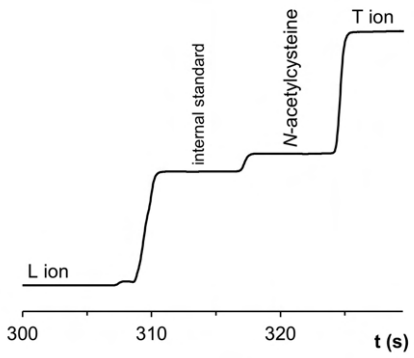
Hradski J., Ďuriš M., Szucs R., Moravský L., Matejčík Š., Masár M., Molecules 26 (2021) 6094.



Masár M., Troška P., Hradski J., Talian I., Microchim. Acta 187 (2020) 448.

Development of new green, miniaturized instruments and methods for the analysis of pharmaceuticals and bio-active substances

Compared to conventional analytical instruments, miniaturized systems require approximately 100-1000 times lower volumes of working solutions and, accordingly, the amount of chemicals. An example of such a system is CE, MCE and mpITP in combination with IMS detection. These stand-alone or combined techniques, such as mpITP-CE-IMS, can be considered environmentally sustainable as their chemical consumption and waste generation are virtually negligible compared to conventional systems. The aim of this research is to verify the hypothesis that these systems routinely reach the performance limits defined by international recommendations for the development of medicines for humans (ICH).

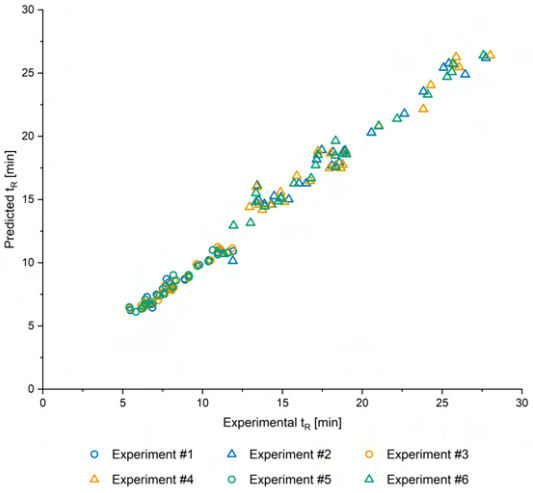


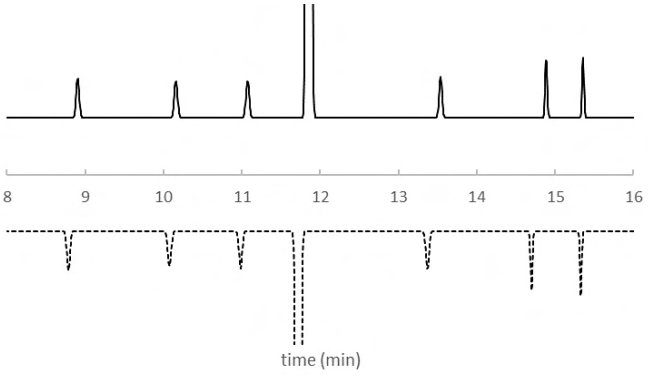
Rudašová M., Masár M., J. Sep. Sci. 39 (2016) 433.

Analysis of Pharmaceutical and Bioactive compounds

Reduction of laboratory activities by implementing computational procedures based on machine learning techniques and artificial intelligence capable of in-silico identification of appropriate experimental conditions

In the last decade, the number of publications dealing with the prediction of retention times in conventional LC based on the so-called Quantitative Structure Retention Relationships (QSRR) has increased rapidly. The aim of this research is to verify the hypothesis of whether electrophoretic and IMS mobility can be predicted by a similar approach. If successful, this approach could be used to reduce laboratory experiments and apply the so-called in-silico selection and optimization of experimental conditions.





Szucs R., Brown R., Brunelli C., Heaton J.C., Hradski J., Int. J. Mol. Sci. 22 (2021) 3848.

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