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Author: Szabolcs Fekete, Julie Schappler, Jean-Luc Veuthey, Davy Guillarme

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# Current and future trends in UHPLC

Szabolcs Fekete, Julie Schappler, Jean-Luc Veuthey, Davy Guillarme \*

*School of Pharmaceutical Sciences, University of Geneva, University of Lausanne, Boulevard d'Yvoy 20, 1211 Geneva 4, Switzerland*

## HIGHLIGHTS

- Ultra-high-performance liquid chromatography UHPLC is the standard LC platform
- Columns packed with sub-2- $\mu\text{m}$  particles come for chiral-LC, SEC, IEX, HILIC and SFC
- Detailed characterization of biopharmaceuticals is an important UHPLC application
- Particle-size reduction and system-pressure increase are technologically difficult
- Superficially porous particles directly improve the kinetic performance of UHPLC

## ABSTRACT

Since its commercial introduction in 2004, there has been a considerable interest in ultra-high-performance (pressure) liquid chromatography (UHPLC), which dramatically increases the throughput of regular HPLC methods. Although the ability to achieve fast separations and good resolution are the main drivers for the increasing use of UHPLC, we describe a number of other trends in this review, such as:

- (1) use of UHPLC technology to perform high-resolution analysis of complex samples;
- (2) development of columns packed with sub-2- $\mu\text{m}$  particles to achieve different chromatographic modes (i.e. chiral LC, SEC, IEX, HILIC, and SFC);
- (3) evaluation of higher pressure drop, higher temperature, smaller particle sizes and sub-2- $\mu\text{m}$  core-shell particles, to further improve kinetic performance;
- (4) use of UHPLC for enhancing the characterization of biopharmaceuticals; and,
- (5) development of UHPLC-MS for applications, including bioanalysis, multi-residue screening, and metabolomics.

### Keywords:

Bioanalysis  
Biopharmaceutical  
Fast analysis  
Fully porous particle  
High-resolution analysis  
HILIC  
Metabolomics  
Superficially porous particle  
UHPLC  
UHPLC-MS

\* Corresponding author. Tel.: +41 22 379 34 63; Fax: +41 22 379 68 08.

E-mail address: [davy.guillarme@unige.ch](mailto:davy.guillarme@unige.ch) (D. Guillarme)

## 1. Introduction

The term UHPLC was originally coined by Jorgenson in 1997 and stands for ultra-high-pressure liquid chromatography. This group was the first to describe the use of nano-columns packed with non-porous 1.0–1.5- $\mu\text{m}$  silica-based particles on a prototype system compatible with very high pressure {up to 4100 bar in 1997 [1] and 7200 bar in 2003 [2]}. Next to the

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