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ACCEPTED MANUSCRIPT

The future of UHPLC: towards higher pressure and/or smaller particles?

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HIGHLIGHTS

- We quantify the potential gain of a future doubling of operating pressure
- We establish expressions for kinetic gain factor
- We take into account the effect of extra-column band broadening
- We construct corrected Knox and Saleem limits
- We demonstrate the need to eliminate connection tubing

ABSTRACT

Simple expressions for kinetic gain factor were established to predict the potential gain in separation speed, efficiency or resolution and peak capacity when moving from a given separation condition (pressure, particle type and size) to optimized conditions. The equations show that the possible gain by moving from 1200-bar to 2400-bar instruments would at most lead to a 40% increase in efficiency and only 20% in resolution or peak capacity, while analysis time would halve. These optimal systems would have to operate with short columns packed with very small particles (0.6–1µm for N = 10,000–25,000), yielding peaks with unprecedentedly small volumes. It would therefore never be possible to realize the full theoretical gain of new investment in pressure due to the instrument contributions. We therefore require radical new designs of chromatographic systems (getting rid of the current need for long connection tubing) to advance the limits of separation power.

Keywords:
Band broadening
Column technology
Impedance
Instrument design
Kinetic plot
Knox and Saleem limit
Particle size
Pressure limitation
Separation power
UHPLC

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1. Introduction

In the past decade, some unexpectedly large jumps in chromatographic separation speed and efficiency have been achieved, by developing columns with sub-2-µm particles [1–3], introducing a new generation of superficially porous particles [2,4], and combining these column-technology advancements with a major increase (factor 3) in maximum system pressure [1,5–7]. Initially, the use of so-called ultra-high-pressure liquid chromatography

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